

CASE SERIES: UPPER AIRWAY OBSTRUCTION IN POST-ACUTE SEQUELAE OF COVID-19 (PASC) INFECTION DUE TO SUBGLOTTIC STENOSIS

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Abstract

Introduction: Post-Acute Sequelae of Covid-19 (PASC) manifestations can lead to upper airway obstruction, especially in patients with a history of intubation. Tracheal intubation can cause damage to the subglottic, the lowest part of the larynx; SARS-CoV-2 infection damages not only the pulmonary system but also the trachea. Subglottic stenosis is an abnormality in the form of narrowing of the airway in the subglottic area. This case series demonstrates that subglottic stenosis needs to be broadly understood as it contributes to PASC and should be considered an airway emergency.

Objective: To emphasize the symptoms and signs of subglottic stenosis in patients with prolonged intubation and to show the correlation between the respiratory tract symptoms and factors contributing to airway obstruction.

Case: We present 2 cases, one month after discharge from the hospital; a 55-year-old man and a 32-year-old man. both came with stridor, dyspnoea, intercostal retractions one month after being hospitalized due to covid-19 infection

Conclusion: There are many symptoms and signs that may occur with shortness of breath, making diagnosis difficult. It is necessary to conduct investigations to establish the diagnosis and find the cause of shortness of breath. Early tracheostomy shortens days on the ventilator, intensive care unit, and hospital and should be considered for patients in the intensive care unit at risk for more than seven days of intubation.

Keywords: COVID-19, PASC, SARS CoV-2, Subglottic Stenosis, Tracheostomy

Introduction

Post-Acute Sequelae COVID-19 (PASC) are symptoms that appear after an acute infection, leaving residual symptoms. Symptoms that last more than 30 days after RT-PCR negative result has been dubbed as long COVID-19, PASC. PASC not only triggers inflammation in the lower respiratory tract but also causes damage in the upper respiratory tract, especially in patients with a history of prolonged intubation. Breathing difficulty in post covid patients is commonly mistaken as lower airway problems. ^{1,2} Persistent inflammation in the trachea causes other complications, such as subglottic stenosis. It is an upper airway abnormality where the subglottic area becomes too narrow.³ Stenosis in the respiratory tract is generally caused by an inflammatory process that occurs due to trauma, intubation, infection, bronchoscopy, external blunt trauma, penetrating trauma, chemical injury, and iatrogenic / post-surgical or other factors including surgical process which lead to mucosal or cartilaginous injury.^{5,6,7} Systemic processes such as laryngopharyngeal reflux, autoimmune diseases, and malignancy also initiate an inflammatory process that leads to scar tissue formation. Intubation is a common emergency procedure during the Covid-19 pandemic and remains as initial therapy for patients with severe presentation or ARDS.⁵ However, the primary cause of subglottic stenosis is prolonged intubation.^{5,8}

Damage occurs from mucosal abrasion or decreased perfusion due to pressure on surrounding blood vessels caused by the cuff.⁸ Etiologic should be able to distinguish between infection, neoplasms, or other systemic disorders. It is important for physician to be able to diagnose.⁸ We present cases of subglottic stenosis in a 55-years-old man and a 32-years-old man with atypical manifestation.

Case 1

A 55-year-old male patient presented with recurrent shortness of breath one month after discharge from COVID-19 treatment. Previously, the patient was treated at the hospital for ± one month until RT-PCR tested negative COVID-19 with a history of intubation for 16 days. Shortness of breath initially came back suddenly, but over time the complaints worsened. Complaints felt continuously throughout the day and interfered with his activities. There is stridor in daily activities and during sleep. In addition, the patient also complained of coughing with phlegm that is difficult to expel and postnasal drip. These symptoms worsened ten weeks after discharge from the hospital. Physical examination showed stridor at inspiration and expiration; supraclavicular, intercostal, and epigastrium retraction; oxygen desaturation to 86%; and respiratory rate was found 26 times per minute. Diagnosis of upper airway obstruction Jackson criteria grade-3 was made, and emergency tracheostomy was done. Breathing difficulty was gone after tracheostomy, and the patient received periodic mucolytic, nebulizer, and suction therapy.

Nasolaryngoscopy found lingual tonsil hypertrophy grade 3. standing secretion in the piriform sinuses and vallecular, minimal arytenoid oedema, visible vocal cords, ventricular oedema, symmetrical movement, closed glottic rhyme, and subglottic stenosis Cotton-Myer grade 3.



Figure 1. Subglottic stenosis Cotton-Myer grade 3 in patient 1.

The patient was also diagnosed with laryngopharyngeal reflux and was treated with Lansoprazole twice daily for two weeks. T-tube installation was done, and the patient can now speak and breathe normally.

Case 2

A 32-year-old man came with shortness of breath. Complaints worsened in the past day before being admitted to the hospital. The patient had a history of SARS-CoV-2 infections and prolonged intubation.

Two weeks after discharge from COVID-19 treatment, the patient complained having breathing difficulty and went to the emergency ward. Physical examination showed stridor at inspiration and expiration; supraclavicular, intercostal, and epigastrium retraction; oxygen desaturation to 80%; and respiratory rate was found 36 times per minute. The patient was diagnosed with upper airway obstruction Jackson criteria grade 3, and a primary tracheostomy was done.

Fibre optic laryngoscopy was done and found hypertrophy posterior commissure, subglottic stenosis Cotton-Myer grade 3.



Figure 2. Subglottic stenosis Cotton-Myer grade 3 in patient 2.

T-tube installation was done, and the patient can now speak and breathe normally.

Discussion

Subglottic stenosis due to prolonged intubation in both patients was confirmed by history taking, physical examination, and fibre optic laryngoscopy. Subglottic stenosis occurred due to trauma of the trachea resulting in oedema, ulceration, and necrosis of the tracheal mucosa.^{11,12} Continuous endotracheal tube (ETT) cuff pressure can stop mucosal blood flow, resulting in mucosal damage and tracheal cartilage pressure necrosis, which leads to membranous-type, cartilage-type stenosis, or a combination of both.^{9,10} ETT cuff with low pressure only causes damage to the mucosa, while the tracheal cartilage structure is still in good condition. If it occurs for a long time, it will cause secondary infection with formation of granulation tissue and connective tissue (fibrosis/cicatrix), whereas if it involves the tracheal cartilage, it can cause cartilaginous stenosis.^{11,12}

SARS-CoV-2 infection causes inflammation of the upper airway, including the trachea. Thus, granulation tissue and subglottic stenosis are more likely to happen in prolonged intubation cases with SARS-CoV-2 pneumonia. Angiotensin-converting enzyme 2 (ACE 2) receptor helps SARS-CoV-2 bind with cells.¹³ This can hence severity of COVID-19 disease cause cell type particularly dense in airway epithelial cells.¹³ Cytokines are released to regulate immunity when inflammation process occurs during SARS-CoV-2 infection. CD4⁺ T-cell-related cytokines regulate the immune response in fibrosis. Fibrosis regulated by T cell 1 (T_{H1}) or T cell 2 (T_{H2}) helper thus differentiated from CD4⁺.¹⁴ This fibrosis formed by excessive collagen, whereas T_{H1} cytokine interferon- γ (INF- γ) lower than T_{H2}-related cytokine interleukin 4 (IL-4) and IL-13. Increasing T_{H2} response might mediate the fibrotic process with stimulated collagen production due to immunologic mechanism by an imbalance of T_{H1} and T_{H2} responses to pathologic fibrosis.¹³

The glottic and supraglottic larynx has variable areas of ciliated respiratory cells, which may explain why subglottis and trachea were profoundly oedematous.¹³ The trachea is formed by cartilaginous structures and surrounded by connective tissue, which contains elastin and collagen.¹³ Patients with SARS-CoV-2 chronic inflammation are prone to airway collapses due to destruction of laryngotracheal cartilage by antibody reaction against type II collagen.¹³

Subglottic stenosis cause obstruction, and one of the causes is the inappropriate size of ETT and prolonged intubation. Ideal ETT size should not be larger and preferably slightly smaller than the tracheal lumen.

There is no critical duration that can negate or reduce the risk of stenosis. Early timing of tracheostomy may accelerate ventilator weaning and free up critical equipment, staff, and units.¹¹

Tracheostomy decision in SARS-CoV-2 pneumonia with prolonged intubation must be personalized based on the patient's conditions. Tracheostomy with supine positions might cause oxygen desaturation in SARS-CoV-2 patients. Thus, 30° - 45° elevation must be considered during the procedure to avoid oxygen desaturation.¹⁵ Anti-coagulant can only

be stopped 6 hours before tracheostomy to reduce the risk of pulmonary emboly. Bleeding risk also increases due to the coagulation factor from the therapy; thus, blunt dissection of the fascia and muscle is preferable to avoid further bleeding. Cauterization must be done if bleeding occurs. An absorbable hemostat can be inserted to enhance tissue coagulation during the tracheostomy procedure. Taper surgical needles must be avoided for suturing to decrease tissue damage and bleeding risk.

Initial changes in the airway mucosa due to persistent ETT pressure can occur within the first 48 hours. After intubation for 2-5 days, the risk of stenosis was 0-2%; the risk was 4-5% after 5-10 days, and the risk was 12-14% if intubation exceeds ten days.¹⁶ The major complaint is shortness of breath and other clinical symptoms such as cough, biphasic stridor, and hoarseness of voice. Shortness of breath is difficult to differentiate from other respiratory disorders.¹⁶ Therefore, history taking of prolonged intubation must be done in PASC patients, as subglottic stenosis can be life-threatening.

Subglottic stenosis is a difficult case from a diagnostic and therapeutic point of view. The treatment for this disease is chosen based on several considerations, including location, types and degree of stenosis, available tools, and the operator's skills and experience. Based on the assessment of the Cotton-Myer grading system, laryngeal stenosis in both patients has reached grade 3, which means laryngeal obstruction reaches 71-99%. Therefore, palliative therapy using a silicone stent was preferred in both patients, making minimal granulation tissue and providing a structure to maintain a patent airway. Silicone stents are easier to place, move, remove, and adjust by the patient.

Conclusion

Subglottic stenosis must be considered in PASC patients with upper airway obstruction, which might often be difficult to differentiate with lower airway problems by the emergency physician. All primary physicians must acknowledge the clinical symptoms of subglottic stenosis, especially in PASC cases, to lower mortality and morbidity. Prolonged intubation must be avoided in patients with SARS-CoV-2 infection to prevent subglottic stenosis and further upper airway complications. Early tracheostomy might be more beneficial in SARS-CoV-2 patients on ventilator.

Competing Interests

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