Acquired Tracheoesophageal Fistula In COVID-19 Patient: A Case Report

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ABSTRACT
Background: Tracheoesophageal fistula is an abnormal connection between the trachea and the oesophagus due to a congenital condition or acquired conditions. The most common causes of acquired TEF include malignancy, trauma, and infection. Patients with acquired TEF have high mortality and morbidity rates due to critical illness and comorbidities.
Purpose: This case report will discuss about how to establish the diagnose and the treatment.
Case report: A 47-year-old female COVID-19 patient with acquired tracheoesophageal fistula
Methods: This case report uses a mixed-methods case study approach. The collection of multiple sources of evidence, using a range of quantitative (audits and analysis of routinely collected medical data) and qualitative techniques (interviews). Evidence-based case reports / case studies of Acquired Tracheoesophageal Fistula in COVID-19 was conducted through Cochrane database, Pubmed.gov, and SpringerLink.
Result: There were 5 articles met the inclusion criteria, stated that to establish the diagnose was with endoscopy and imaging. Management of acquired TEF in COVID-19 patients is generally reconstructive, but there is a report that stated fistula closure spontaneously.
Conclusions: The gold standard for the diagnosis of TEF is obtained by endoscopy. The mortality and morbidity of TEF patients are high because of the critical illness and comorbidities.

Keywords: *Acquired tracheoesophageal fistula, and COVID-19*

INTRODUCTION

Tracheoesophageal fistula (TEF) is a pathological condition with an abnormal connection between the trachea and the oesophagus due to a congenital condition or acquired conditions. Congenital tracheoesophageal fistula is caused by incomplete development of the tracheoesophageal septum and can occur between the 4th and 8th week of the embryonic period when there is abnormal tracheal growth. Symptoms of TEF are generally caused by aspiration of food or drink particles which then lead to pulmonary complications that can be life-threatening.[1]
The most common causes of acquired TEF include malignancy, trauma, and infection. The cause of acquired TEF due to mediastinal malignancy is about 50%. Causes of acquired TEF due to direct trauma can be sharp or blunt trauma, corrosive chemicals, inhalation burns, or esophageal trauma from swallowing button batteries. Other causes of acquired TEF include trauma due to medical or iatrogenic procedures such as a history of previous tracheal or esophageal surgery, insertion of an esophageal stent, tracheal or esophageal endoscopy, transoesophageal echocardiography, and use of an endotracheal tube (ETT) for intubation and percutaneous tracheotomy.[2] Associated trauma with the ETT cuff contributing to acquired TEF in most groups other than malignancy.[3]

Other factors accompanying conditions such as poor general health, respiratory tract infections, hypotension, diabetes mellitus, nasogastric tube (NGT) use, and prolonged intubation can increase the likelihood of acquired TEF. Infections that can cause acquired TEF are candida, cytomegalovirus (CMV), granulomatous infections such as tuberculosis, varicella zoster, and secondary infections associated with HIV.[1,4]
A multicentre study in 2021 in the United States reported that COVID-19 patients who were treated in the intensive care unit (ICU) and required invasive mechanical ventilation (IMV) had the three highest comorbid prevalences, including hypertension 51%, obesity 35%, and diabetes 30%.[5] An Italian study in 2020 reported that COVID-19 patients receiving IMV had full-thickness tracheal lesions until TEF was obtained.[6]
The purpose of this evidence-based case report is to report a case of acquired TEF in an adult female patient infected with COVID-19 with several comorbidities.

CASE REPORT

A 47-year-old female patient came to the OPD ORL-HNS Dr. Soetomo Hospital on 18 November 2020, was consulted by the Anaesthesia department with the main complaint of coughing accompanied by shortness of breath every time he swallowed lasted 17 days, and this complaint feels like it is getting worse and worse. Complaints are accompanied by discharge from the neck of the former tracheotomy hole. The liquid that comes out is saliva mixed with food/drink without the presence of blood.

The patient had been hospitalized for 26 days in the Special Isolation Room (SIR) (a grey area in figure 1) due to COVID-19 infection and continued 45 days in the ICU. The history of the disease course and the actions taken on this patient can be seen in Figure 1 below.

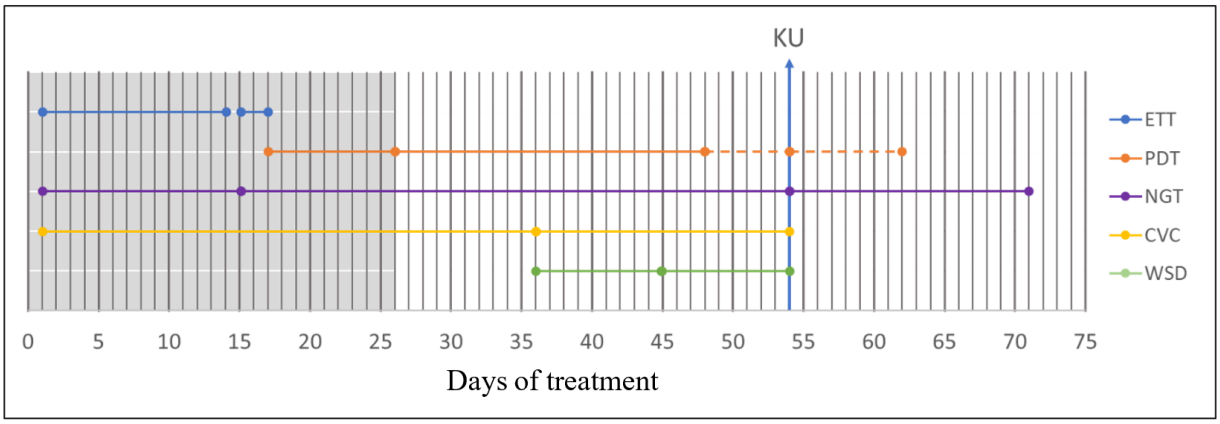

Figure 1. Timeline graph of actions performed during treatment in SIR (grey box) and ICU. ETT: endotracheal tube; PDT: percutaneous dilatational tracheostomy; NGT: nasogastric tube; CVC: central venous catheter; WSD: water seal drainage chest tube; KU: The main complaint came first.

History of using non-invasive ventilation (NIV) for 1 day at SIR and then intubated with an endotracheal tube (ETT) and a ventilator for a total of 15 days. The patient was extubated for 1 day on the 14th day of treatment, but he was re-intubated the next day due to unstable oxygenation. After that, Percutaneous Dilatational Tracheostomy (PDT) was performed because the pneumonia worsened. PDT was used for 45 days with a ventilator for 31 days and 14 days without a ventilator, and then decannulation was carried out after undergoing 62 days of treatment.

Monitoring of cuff pressure, both ETT and PDT, cannot be performed due to the limitations of the equipment that can be used in SIR (a grey area in Figure 1). However, once the patient has been transferred to the ICU, PDT cuff pressure monitoring can be performed. The first cuff pressure measured in the ICU was recorded as 80cmH2O. While in the ICU, the PDT cuff pressure was monitored at a maximum of 30cmH2O and a maximum cuff volume of 8ml.

History of central venous catheter (CVC) placement for 53 days, NGT for 70 days, water-sealed drainage (WSD) chest tube for 18 days. The patient had experienced septic shock for 5 days and responded well to culture-appropriate antibiotics and drugs to regulate hemodynamic. Complaints of choking and shortness of breath appeared shortly after the PDT and NGT were removed on the 54th day of treatment (blue arrow in Figure 1), so it was decided to put the PDT and NGT back in. The patient was discharged from the hospital after undergoing treatment for 71 days with the NGT attached.

The patient has history of type 2 Diabetes Mellitus since more than five years ago, controlled with taking glimepiride anti-diabetic drugs (OAD) and metformin. During treatment in SIR and ICU, OAD was replaced with insulin, namely Levemir and Novorapid.

When the patient first came, the results of the physical examination conducted at the OPD ORL-HNS Dr. Soetomo Hospital found that her general condition was adequate, her consciousness was compos mentis, her weight was 55 kg, and her height was 155 cm. Vital signs within normal limits. The local status of the ear and throat examination was within normal limits. On nasal examination revealed that the NGT was installed in the right nostril, functioning well, both nasal cavities were spacious, and there were no secretions. On neck examination, scar tissue from PDT installation was found, there is a clear and thick secretion that looks like saliva, no blood, and pussy/pus. CVC scar tissue was in good condition, with no bleeding or hematoma (Figure 2).

Figure 2. Scar tissue from the PDT installation shows salivary secretions (green arrow). Good CVC scar tissue (yellow circle).

Patients diagnosed with suspicion of non-malignant acquired TEF. The patient is planned for trans nasal esophagoscopy (TNE) examination, Multislice Computerized Tomography (MSCT), and 3D airway reconstruction. TNE examination was carried out when the patient arrived for the second time, 10 days after the first examination to the OPD ORL-HNS Dr. Soetomo Hospital. The results show a fistula that connects the lumen of the esophagus to the trachea with the broadest diameter estimated at 1 cm, the edges of the fistula are smooth, located 25-26 cm from the nostril (Fig. 3). Smooth vocal cords, symmetrical shape, symmetrical movement, airy airway, normal epiglottis.

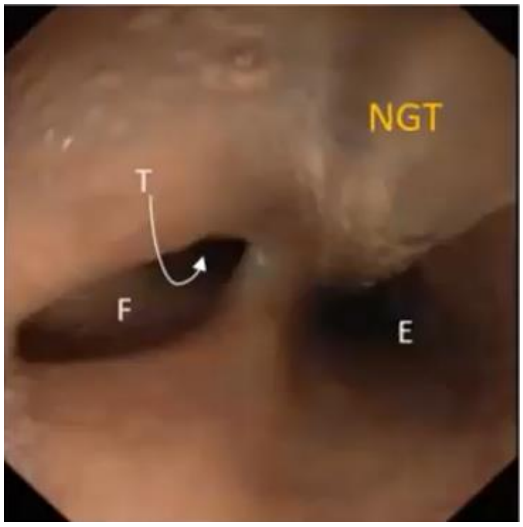

Figure 3. Visible fistula (F) that connects the esophagus (E) with the trachea (T), NGT in the lumen of the esophagus.

MSCT examination of the neck without contrast and 3D airway reconstruction was performed 33 days after the first arrival at the URJ ENT-KL, with the results showing a defect of ±0.4 cm along ±1.1 cm as high as Vertebra Cervicalis (VC) 7 – Vertebra Thoracalis (VTh) 1 on the esophagus that connects the trachea and the esophagus. The trachea appears to be pulled to the right (Fig. 4).
Patients diagnosed with non-malignant acquired TEF with a history of COVID-19 pneumonia, *acute respiratory distress syndrome* (ARDS), ventilator-associated bacterial pneumonia, septic shock, and type 2 diabetes mellitus. Case discussions were held between the departments of ENT, Cardiothoracic Vascular Surgery (CTVS), Radiology, and Anaesthesiology to plan trachea-esophageal reconstruction surgery with an external cervicotomy approach and partial sternotomy on January 26, 2021.

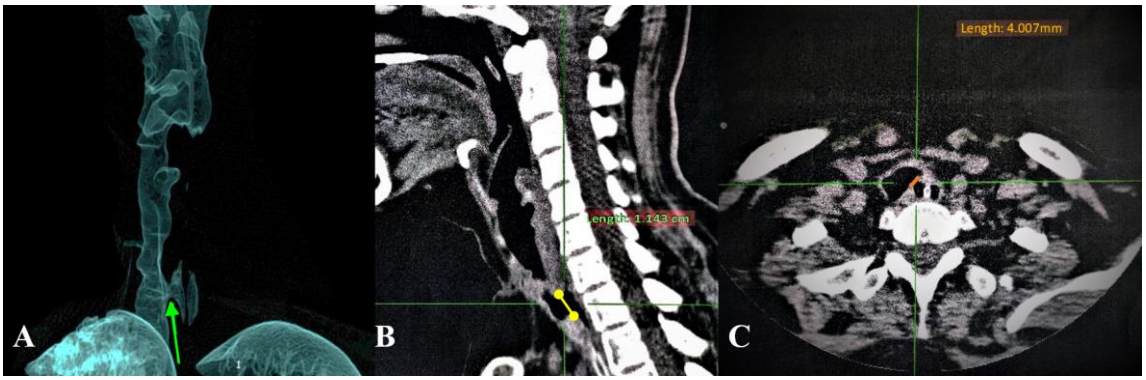

Figure 4. 3D airway reconstruction and MSCT; A. 3D airway showing a trachea-oesophageal fistula (green arrow); B. Sagittal section: 1.143cm long defect located at VC7-VTh1 level (yellow line); C. Axial section: 4,007mm defect on the right anterolateral side of the esophageal wall (orange line). The trachea appears to be pulled to the right side.

During the process of preparing for reconstructive surgery, the patient's condition worsened 60 days after leaving the hospital. The patient came to the ER complaining of shortness of breath and a severe cough accompanied by thick green sputum. Oxygen saturation on arrival was 60%, with NIV increased only 80%. The patient underwent a COVID-19 PCR swab with no noticeable results. The patient's condition then continued to deteriorate until 2 days later he died.

CLINICAL QUESTION

What is the golden standard to diagnose acquired TEF?

METHODS

A structured literature search using keyword "tracheoesophageal fistula" AND "COVID-19" was conducted on Cochrane, PubMed.gov and SpringerLink. The searching was conducted on August 10th 2022. 32 articles were found, and further selection is based on inclusion and exclusion criteria.
The inclusion criteria were: Acquired tracheoesophageal fistula in COVID-19 patient, written in English, and full text available. The exclusion criteria were: case other than acquired tracheoesophageal fistula, case other than COVID-19, and duplicate studies.

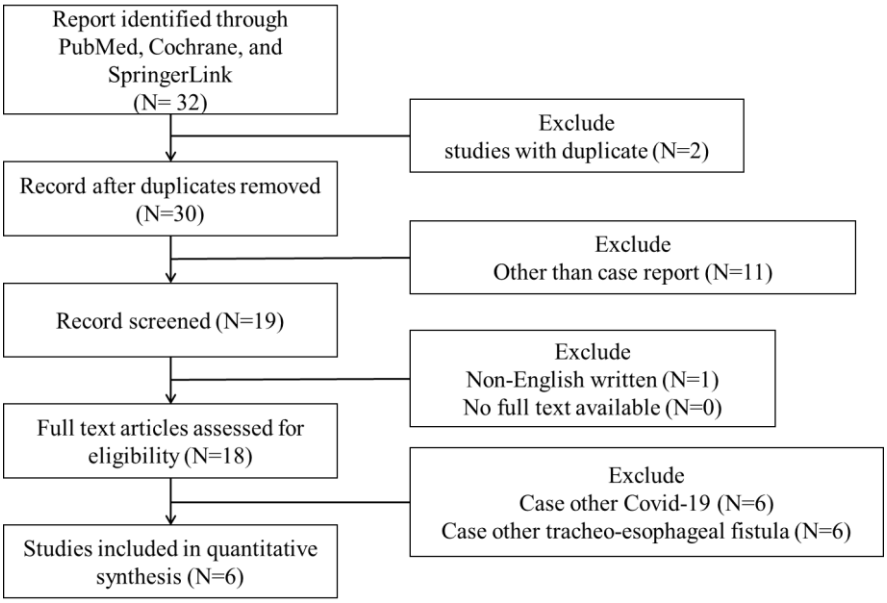

Figure 5. Search terms and selection process of publication (PRISMA flowchart).

RESULT

The literature search result on Cochrane database, PubMed.gov and SpringerLink, 32 studies obtained. Six studies met the criteria and relevant with scientific question were studied and thus we perform a critical study (Table1).

Rosati, et al., (2021) reported a case of 52-year-old male patient, with history of obesity, diabetes and tested positive for COVID-19. After 2 days, the patient was transferred to ICU and intensive respiratory treatments was started including prone position, 20% of the day on average during the first week. On hospital day 25, the patient developed thoracic subcutaneous emphysema. A chest X-ray showed bilateral pneumothorax and subcutaneous emphysema. A chest CT scan confirmed the presence of a large pneumomediastinum and an overinflated tracheal tube cuff. On hospital day 28, massive subcutaneous bilateral emphysema in the cervical and anterior thoracic region and massive air inflation into the NGT occurred.
A chest X-ray revealed overdistension of the stomach. A tracheoesophageal fistula (TEF) was thus suspected. Bronchoscopy confirmed a TEF of approximately 2 cm located 3 cm distal to the vocal cords and 5 cm proximal to the carina and an enlarged trachea lumen. Under direct bronchoscopy, the endotracheal tube was placed distal to the TEF. Surgery was scheduled to repair the tracheal and esophageal tears while performing a tracheostomy.
An upper GI endoscopy was performed to properly localize the esophageal fistula, which was in the anterior esophageal wall approximately 4 cm distal to the upper esophageal sphincter (UES).
Roomi, et al., (2020) reported a case of 53-year-old female presented to the hospital with hypoxemic respiratory failure caused by COVID-19 pneumonia. She got intubated and her hospital course was complicated by ARDS. She got extubated by the end of the third week but reintubated for persistent hypoxemia two days later. She was on the pressure control mode of ventilation with positive end expiratory pressure (PEEP) of 16, Inspiratory Pressure (Pi) of 19 and peak pressure of 35. Suddenly, she developed hypoxemia and gastric distension on the same ventilator settings and her peak pressure dropped to 22. The X-ray of the abdomen was normal. Sudden dropping of peak pressure prompted the clinician to get computerized tomography (CT) scan of the neck which revealed trachea-esophageal fistula.
Pereira, et al., (2021) reported a case of 62-year-old female patient, with history of deep venous thrombosis, dyslipidaemia, and SARS CoV-2 associated pneumonia with severe hypoxemic respiratory insufficiency. The patient was admitted to ICU and intubated. The patient required neuro-muscular blockade and three 16-hour sessions of prone position (on day 9, 12 and 15 of IMV). Additionally, the patient underwent 10 days of intravenous (IV) 6 mg dexamethasone, therapeutic thrombo-prophylaxis with enoxaparin and broad-spectrum antibiotics for a ventilator associated bacterial pneumonia and secondary bacteriemia.
On day 18 of IMV, an endotracheal tube cuff leak was identified. A cervicothoracic computerized tomography (CT) scan was performed. This exam revealed a dilated trachea, with a maximal transverse diameter of 53 mm. In a second CT scan on day 22 of MV, performed with a deflated cuff, the trachea remained dilated. Additionally, a 20 mm × 10 mm communication between the posterior tracheal wall and the oesophagus was identified, consistent with the diagnosis of TEF.
TEF management was initially conservative. The nasogastric tube (NGT) was replaced by a percutaneous endoscopic gastrostomy (PEG) on day 24 of IMV for nutritional support. A percutaneous tracheostomy was performed on day 33 of IMV. Further complementary exams were taken, third CT-scan, bronchoscopy, and upper gastrointestinal endoscopy. Dimensions remained stable, as there was no evidence of spontaneous healing and closure of the fistula.
Cuaño, et, al., 2021 reported a case of previously healthy pregnant woman was diagnosed with COVID-19 pneumonia and was subsequently intubated with no known comorbidities. Throughout the course of her illness, the patient was treated for recurrent bouts of pneumonia. A high-resolution chest and neck CT scan confirmed the presence of a tracheoesophageal fistula (TEF), which may have been caused by the presence of the overinflated endotracheal cuff, prolonged steroid use, hypoxic injury, and possible direct injury of the tracheal mucosa from COVID-19 itself. Unfortunately, the patient succumbed to infection prior to definitive repair.
García-Herreros, et, al., (2020) reported a case of 41-year-old male tested positive for COVID-19, presented with fever, cough and progressive dyspnoea over a 24h period with rapid progression to acute respiratory failure requiring emergency tracheal intubation. COVID-19 viral pneumonia and ARDS developed. Mechanical ventilatory support in the intensive care unit was carried out using a prone ventilation strategy and high-volume and low-pressure endotracheal tube cuffing. After 10 days of ventilatory support, the patient's condition improved, and he was extubated with no adverse event reported. Thirty days post-extubation, the patient began complaining of coughing, difficulty swallowing and choking on liquid intake.
Neck and thoracic computed tomography imaging showed post-intubation tracheoesophageal fistula (PITEF) at the level of C5–C6 and several tracheal stenoses. Bronchoscopy identified the orifice-defect of PITEF measuring 0.8 × 0.7cm on the smooth posterior membranous wall 3–4cm from the cricopharynx.
Negaresh, et, al., (2021) reported a case of 44-year-old woman with 3 years of Behcet's disease and using prednisolone 5 mg/day for its treatment experienced a severe COVID-19 infection. Since the patient's condition gradually deteriorated and her oxygen saturation decreased to 80%, she was transferred to the ICU. On the fourth day, she experienced lethargy, tachypnoea, respiratory distress, and decreased oxygen saturation. She was thus maintained at a supine position, sedated, and intubated. The patient's family did not give consent for tracheostomy.

After extubation, she complained of hoarseness and coughing while swallowing fluids (not solid foods). Chest CT scan revealed signs of TEF in the proximal region of the thorax with obliteration of fat plane 30 mm distal to hypopharynx between tracheal and oesophagus and indentation in posterior wall of trachea. The patient underwent bronchoscopy. The results showed an 8 mm perforation in the trachea 3 cm from the vocal cords on the left side of the posterior membrane with a one-way valve to the trachea.

Table 1. **Literature review in the form of case report**

No	Writer-Journal	Publication Type	Population / Patient	Intervention / Index / Indicator	Comparator	Outcome
1	Rosati, et al., Case Rep Surg, 2021	Case Report	52-year-old male patient, with history of obesity and diabetes	Chest X-ray, Neck CT scan, Bronchoscopy	-	Chest X-ray revealed overdistension of the stomach. Neck CT scan showed overinflated tracheal tube cuff. Bronchoscopy confirmed a TEF of approximately 2 cm located 3 cm distal to the vocal cords and 5 cm proximal to the carina and an enlarged trachea lumen
2	Roomi, et al., Chest, 2020	Case Report	53-year-old female	Abdominal Xray, Neck CT scan	-	The X-ray of the abdomen was normal. Neck CT scan revealed trachea-esophageal fistula
3	Pereira, et al., Saudi J Anaesth, 2021	Case Report	62-year-old female patient, history of DVT and dyslipidaemia	Serial Cervico-thoracic CT scan, broncho-fibroscopy, Esophagoscopy	-	CT scan showed 20 mm × 10 mm communication between the posterior tracheal wall and the esophagus. Endoscopic showed the same result
4	Cuaño, et al., BMJ Case Rep, 2021	Case Report	post-caesarean section female patient,	Serial Chest x-ray, Neck CT with contrast	-	A defect in the posterior tracheal wall and/or anterior oesophagus was seen, measuring 1.5×1.4cm (Craniocaudal×Width), along with a new pneumothorax on the left upper hemithorax and accompanying compression atelectasis of the left upper lobe.
5	García-Herreros, et al., Ann R Coll Surg Engl 2021	Case Report	41-year-old male, no previous medical history.	Neck and Thoracic CT scan, bronchoscopy	-	Neck and Thoracic CT scan showed PITEF at the level of C5–C6 and several tracheal stenoses. Bronchoscopy identified the orifice-defect of PITEF measuring 0.8 × 0.7cm on the smooth posterior membranous wall 3–4cm from the cricopharynx.
6	Negaresh, et al., Clin Case Rep, 2021	Case Report	44-year-old woman with 3 years of Behcet's disease and using prednisolone	Chest CT scan, esophagography with contrast, bronchoscopy	-	Chest CT scan revealed TEF in the proximal region of the thorax with obliteration of fat plane 30 mm distal to hypopharynx between tracheal and esophagus with indentation in posterior wall of trachea Esophagography revealed aspiration of the contrast and the diffusion of edible contrast material into the trachea, right and left bronchi, and lobar branches Bronchoscopy showed an 8 mm perforation in the trachea 3 cm from the vocal cords on the left side of the posterior membrane with a one-way valve to the trachea.

DISCUSSION

The patient, in this case, was 47 years old and female, Javanese, Mongoloid-Malay race. This follows the literature that says that acquired TEF can occur in individuals of all ages; however, elderly individuals who have used a ventilator due to respiratory failure are more at risk of acquiring TEF. There is no reported racial predisposition associated with the incidence of acquired FTE.[3] Research in Italy in 2021 stated that female

COVID-19 patients can increase the incidence of this case.[7] This is correspond with a case report by Roomi (2020), who reported a 53-year-old woman with a similar condition.[8]
In this case, the complaints that arise are choking shortly after drinking/eating and saliva coming out through the PDT stoma wound. The first complaints appeared shortly after the PDT and NGT were removed. Because of the suspicion of acquired TEF, the NGT is re-installed to prevent gastric distension and for nutritional intake, and the patient is prohibited from swallowing saliva.
This condition follows the literature, explaining that the clinical presentation may vary among patients. Symptoms experienced by the patient include coughing when swallowing (Ono's sign), acute dysphagia, shortness of breath, hoarseness, lung infection, and pneumonia. Other clinical features include chest pain, fever of unknown origin, haemoptysis, and aspiration.[13]
Patients in critical cases may experience severe respiratory distress. The acquired TEF is potentially life-threatening because it can repeatedly contaminate the trachea, causing tracheobronchial contamination, resulting in pneumonia, pulmonary sepsis, and impaired patient nutrition.[13] Case report in United States of America notify that using of IMV is suspected of causing acquired TEF if the patient experiences sudden desaturation, gastric distention, or a decrease in peak pressure without any change in ventilator settings.[8] However, this case is not matched with the previous literature because previously, NGT was installed, so gastric distention was not obtained. There are other signs but become not typical because the symptoms of COVID-19 covering up as the primary disease.
This patient is infected with COVID-19 with severe ARDS symptoms, so she requires IMV treatment in the ICU and SIR with several high-risk actions that can lead to acquired TEF. These actions include using ETT for 15 days, then continued with PDT for 32 days with IMV, then 14 days without IMV, NGT during treatment, CVC for 53 days, WSD for 18 days, and the duration of treatment is more than 70 days lead to acquired TEF. Some literature reports that for COVID-19 patients treated in ICUs worldwide, tracheotomy is postponed until the patient no longer requires IMV, especially for prone patients who have tested negative for the SARS-CoV2 virus. This is due to the high risk of cross-infection among medical personnel due to a prolonged viral load in the trachea. The delay in tracheotomy is about 3-4 weeks, with a high risk of tracheal lesions that can cause acquired TEF.[14]
Multicentre research in the United States reported the results of 8 studies. The five studies found that 21% of COVID-19 patients required ICU care with an average duration of treatment of 7,78 days. According to 18 studies, the prevalence of IMV use in the ICU in COVID-19 patients is 69%, with a mortality rate of 43-74%, and the average duration of IMV use is 10,12 days. The three most common comorbid prevalences are hypertension (51%), obesity (35%), and diabetes (30%).[5] Research in Italy reports that as much as 33% of COVID-19 patients receiving IMV had full-thickness tracheal lesions and 13% had acquired TEF. IMV was used for 22 days on average in COVID-19 patients, with orotracheal intubation a median of 10 days and use of a tracheotomy cannula an average of 11 days.[6]
High-compliance cuff ETT helps prevent oxygen leakage as well as a pulmonary aspiration in IMV use but can result in direct pressure transmission to the tracheal wall surrounding the ETT cuff. Erosion of the trachea and esophagus walls by an ETT cuff or tracheotomy results in the development of non-malignant acquired TEF, especially if an NG tube is inserted. ETT cuff volume and pressure require consistent monitoring to avoid injury to the trachea.[15] The incidence of acquired TEF due to ETT in mechanically ventilated patients is 0,3% - 3%, while that due to percutaneous tracheotomy is 0,5%. The main predisposing factor that causes necrosis and fistula formation is tracheal wall ischemia due to high ETT cuff pressure. The use of a high-volume, low-pressure ETT cuff has reduced the incidence of complications of acquired TEF.[1,3]
Due to the limitation of equipment and pulmonary compliance are poor, so in this case, the cuff volume was increased to 10-12 ml with a ventilator setting using Synchronized Intermittent Mandatory Ventilation - Positive End Expiratory Pressure (SIMV-PEEP). The first time PDT cuff pressure measured in the ICU was recorded at 80 cmH_2O, so it is assumed that for 25 days, the ETT and PDT cuff pressure in SIR was around 80 cmH_2O with a volume of 10 ml. While in the ICU, the PDT cuff pressure was monitored at a maximum of 30 cmH_2O and the cuff volume was not more than 8 ml. This report is in line with the previous literature that the suspicion of trauma to the trachea due to cuff pressure that exceeds the recommended limit causes the occurrence of acquired TEF.
Previous literature recommends regular inflation-deflation of the ETT cuff every few hours; however, this method has not been shown to reduce the risk of tracheal injury and may even increase the risk of aspiration. An ETT cuff pressure of more than 30 cmH_2O compresses the mucosal capillaries and impairs perfusion in the tracheal wall. Ischemic damage to the trachea is affected by the balance between mucosal perfusion pressure and the pressure exerted by the cuff. ETT cuff pressures that exceed 40 cmH_2O (perfusion pressure on the tracheal and submucosal mucosa) can cause erosion, mucosal ischemia and/or necrosis, loss of ciliary mucosa, ulceration, bleeding, tracheal stenosis and tracheoesophageal fistula. The initial lesion that appears is tracheitis without ulceration, followed by erosion of the tracheal mucosa and exposure to cartilage.[3]

Complete occlusion occurred at 50 cmH_2O, so the cuff pressure is generally recommended not to exceed 20 cmH_2O. Monitoring the ETT cuff pressure alone is insufficient, as tracheal damage and increased cuff volume can occur even when the cuff pressure is kept within the desired pressure range. The cuff volume should ideally not exceed 6 to 8 ml. Caution should be exercised in inflating the ETT cuff > 10 ml, which can cause tracheal injury.[3,15]

Tracheal mucosal damage due to hypoxia is seen from the lower PaO_2/FiO_2 ratio in the second week of IMV compared to the non-COVID-19 group. The average PaO_2/FiO_2 ratio of COVID-19 patients in week 2 was 118, compared to the control group was 156.[6] The hypoxic condition in this case was caused by ARDS, which was indicated by the PaO_2/FiO_2 ratio reaching 139 during the third week of IMV use and the state of septic shock that occurred.

Research in the United States of America in 2020 explain that the SARS-CoV-2 virus was found in tracheal epithelial cells and extracellular mucus in the tracheal lumen from 14 autopsies characterized by a low cycle threshold. High viral replication in the tracheal epithelium can cause mucosal lesions suspected of causing a local inflammatory reaction in the tracheal area.[16] In this patient, only a nasopharyngeal swab was performed, not a tracheal swab PCR.

In this case, PDT was performed using the Ciaglia Serial Dilatation Technique after 15 days of IMV treatment. However, due to poor lung compliance due to ARDS due to COVID-19, the PDT cuff continues to be developed to provide adequate oxygenation and prevent oxygen leakage. In this case, the total use of IMV was 62 days. According to some literature, both conventional and PDT surgical techniques, tracheotomy can be associated with rare but life-threatening complications, such as bleeding, pneumothorax, stomal infection, tracheal or esophageal laceration, and even tracheo-cutaneous and/or tracheoesophageal fistula.[17]

This patient was also placed on a CVC to control long-term fluid and nutritional balance during treatment. The CVC was installed on the 1st day of treatment, reinserted on the 36th day, and then removed on the 54th day of treatment. CVC itself has the risk of causing TEF to be obtained. This is consistent with a case report in Sudan which explains that CVC insertion can cause iatrogenic TEF complications. Although the main complaints of TEF are obtained, such as productive cough and choking, especially when eating/drinking due to CVC, the patient complains immediately after installing the CVC.[18] In the case of COVID-19, this complaint may be disguised by complaints due to COVID-19 itself. Thus, the suspicion of TEF was obtained in this patient because CVC insertion could not be ruled out.

In this case, although the patient does not have malnutritional status (BMI = 22.9), there was a history of diabetes for more than five years with the use of anti-diabetic drugs (OAD) and was replaced with insulin during hospitalization. ARDS due to COVID-19, ventilator-acquired pneumonia (VAP), and hemodynamic compromise due to septic shock were present in this patient. This patient also had an NGT inserted during the first intubation within 62 days of insertion. This condition also increases the feasibility of acquired TEF following the previous literature. Predisposing factors for the occurrence of acquired TEF in addition to prolonged use of IMV include poor general condition, poor nutritional status, respiratory tract infections, restless/awakened patients when intubated, diabetes, steroid therapy, and low oxygen delivery to tissues/decreased tracheal mucosal blood flow which can be caused by hypotension, shock states, anaemia, hypoxemia, and metabolic acidosis. Additional mechanical factors, such as placement of a nasogastric tube, may increase the risk of TEF in patients undergoing prolonged tracheal intubation due to compression of the trachea-esophageal mucosa such as sandwich bread, compression between the ETT cuff anteriorly and the NGT posteriorly.[1,2,15]

In this case, TNE was performed to confirm the diagnosis of acquired TEF, then continued with MSCT examination and 3D airway reconstruction to measure and project the position of the fistula with the surrounding tissue to estimate the appropriate surgical approach. This case is consistent with the previous literature that the diagnosis of acquired TEF can be made using a high-resolution CT scan (HRCT), barium contrast esophagogram, or endoscopy.[1,3] Endoscopy is the best diagnostic method because it allows direct visualization.[4] In this patient, no contrast esophagogram was performed because of the high risk of aspiration. The results of the TNE examination showed a fistula connecting the lumen of the esophagus to the trachea with the broadest diameter estimated to be 1 cm, the edge of the fistula smooth, located 25-26 cm from the nostril. The results of the MSCT examination of the neck without contrast and 3D airway reconstruction showed a defect of ±0.4 cm along ±1.1 cm as high as Cervical Vertebra (VC) 7 - Thoracal Vertebra (VTh) 1 in the esophagus that connects the trachea and esophagus. This case is in line with the previous literature that acquired TEF, both malignant and non-malignant, 52-57% of the fistula locations are between the esophagus and the trachea, 37-40% between the esophagus and the left or right main bronchus, and about 3–11% between the esophagus and the lung parenchyma. Endoscopy is the best diagnostic method for diagnosing acquired TEF because of direct visualization. Reflux of esophageal contents into the trachea causes aspiration, respiratory distress, infection, pneumonia, and possibly airway obstruction. Fistula size correlates with the extent of airway contamination.[19]

Patients with acquired TEF have high mortality and morbidity rates due to critical illness and comorbidities suffered by the patient. The most common and fatal complications of acquired TEF are pulmonary

complications. This complication occurs due to respiratory tract contamination which causes recurrent pneumonia, acute lung injury, ARDS, lung abscess, malnutrition, bronchiectasis due to repeated aspiration, respiratory failure, sepsis, and death.[3] While preparing for fistula reconstruction surgery, the patient came to the Emergency Department due to shortness of breath because of severe pneumonia. Complaints of shortness of breath and a severe cough accompanied by thick green sputum, 60% oxygen saturation on arrival, with NIV increasing only 80%, then a COVID-19 PCR swab was performed with no detectable results. The patient's condition continued to deteriorate until she died 2 days later. Suspected cause of death was post-COVID-19 pneumonia aggravated by repeated reflux aspiration.

CONCLUSION

In COVID-19 patients treated with invasive mechanical ventilation need to be aware of the existence of tracheal lesions, especially acquired tracheoesophageal fistula. Typical symptoms such as Ono's sign, medication history, and supporting comorbidities are also a consideration in making the diagnosis. The gold standard for the diagnosis of TEF is obtained by endoscopy. Management of non-malignant TEF in COVID-19 patients is generally reconstructive surgery if the patient's condition supports surgery. The mortality and morbidity of TEF patients are high because of the critical illness and comorbidities suffered by the patient.

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