

Review Article

Esophageal achalasia, an unexpected complication of COVID-19 post palatoplasty: a case report and literature review

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ABSTRACT

The COVID-19 pandemic, caused by SARS-COV-2, has led to significant mortality worldwide. Despite the declaration in May, 2023 by the World Health Organization (WHO), that the COVID-19 pandemic is no longer a public health emergency of international concern, some survivors are experiencing post-infection complications, including esophageal achalasia. Esophageal achalasia is a rare neurodegenerative disorder characterized by impaired esophageal motility and lower esophageal sphincter dysfunction. This study reviews the literature to explore the association between COVID-19 and achalasia and also presents a case of a 9-month-old child diagnosed with achalasia following COVID-19 infection; a unique occurrence in a young child. This study comprises a case report and a literature review. Clinical data for the case report was collected from medical records, while the literature review included a search of electronic databases from January 2020 to October 2023. Keywords related to COVID-19 and esophageal achalasia were utilized to conduct a search in electronic databases resulting in 9 selected articles. This study underscores the emerging concern of esophageal achalasia as a post-infection complication of COVID-19. It provides a unique case of a young child developing achalasia after COVID-19 infection and reviews the limited literature on this association. Further research is needed to understand the underlying mechanisms and potential preventative measures for this rare complication in COVID-19 survivors.

Keywords: Esophageal achalasia, COVID-19, SARS-Cov-2, Cleft palate

INTRODUCTION

COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) has resulted in the dramatic loss of thousands of lives around the world.¹ Even though the World Health Organization (WHO) declared on 05 May 2023, that the COVID-19 pandemic is no longer considered a public health

emergency of international concern (PHEIC) and is now classified as a persistent health problem, certain individuals who survived SARS-COV-2 infection continue to grapple with enduring health complications associated with the disease. One of the unexpected reported complications of this infection is esophageal achalasia.² The term “achalasia” originates from the Greek word a-khalasis, meaning lack of relaxation. It is a neurodegenerative disorder characterized by the absence

of esophageal peristalsis and a reduced ability of the lower oesophageal sphincter (LES) to relax in response to swallowing.³ At the gastroesophageal junction, these anomalies often lead to a functional blockage. It is a rare disease with a reported worldwide annual incidence of 0.5 cases per 100,000 people.^{4,5} Anyanwu et al and Ezemba et al have reported the incidence of achalasia to be about 3 to 6 cases per year.^{6,7} There is no race or gender predilection for the disease.⁵ Both genders have been reported to have a bimodal distribution in the age-specific incidence of achalasia, with early onset between the ages of 20 and 40 and late onset after the age of 60.^{8,9}

Research into the association between SARS-COV-2 infection and achalasia is ongoing and less than 50 cases have been reported worldwide.^{2,10-15} These reports suggest that there may be an association between SARS-COV-2 infection and development of achalasia, however universal consensus on this association is yet to be established. The purpose of this study is to report a case of a 9 month old boy who developed achalasia after COVID-19 infection diagnosed shortly after a palatoplasty procedure. The study also reviews the literature on the association between SARS-COV-2 infection and development of achalasia.

METHODS

Study design

This article presents a case report and a literature review. The case report involves a retrospective analysis of clinical data, diagnostic procedures, treatment, and outcomes for a 9-month-old child diagnosed with achalasia following COVID-19 infection and palatoplasty. The literature review synthesizes relevant studies exploring the potential association between COVID-19 infection and the development of achalasia.

Data collection

For the case report, clinical data were collected from the medical records of the pediatric surgical ward at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC). This included pre-operative assessments, surgical procedures, post-operative

complications, diagnostic imaging results, COVID-19 test results, treatment interventions, and follow-up records.

Literature review

The literature review involved a comprehensive search of electronic databases including PubMed, Cochrane database of systematic reviews and Cochrane central register of controlled trials. Articles published between January 2020 and October 2023 were included in the review. The inclusion criteria encompassed studies reporting cases of achalasia following COVID-19 infection. The following keywords were used in the MeSH: ("COVID-19"[Mesh]) AND "Esophageal Achalasia"[Mesh], ("SARS-COV-2"[Mesh]) AND "Esophageal Achalasia"[Mesh].

Data analysis

Clinical data was extracted from the patient’s medical records to provide a detailed description of the patient’s medical history, clinical presentation, diagnostic procedures, treatment interventions, and clinical outcomes.

In the literature review, retrieved articles were screened based on titles and abstracts for relevance to the research objective. Full-text articles meeting the inclusion criteria were critically reviewed and analyzed for key findings, methodological quality, and relevance to the association between COVID-19 and esophageal achalasia. Data from selected studies were extracted, categorized, and synthesized to provide a comprehensive overview of the current state of knowledge regarding the potential relationship between COVID-19 infection and achalasia development.

RESULTS

Electronic database search on PubMed, Cochrane database of systematic reviews and Cochrane central register of controlled trials returned a total of 13 search results. 5 articles were selected after removal of non-specific articles and duplicates. References of included articles were also assessed and 4 articles were included from their references (Figure 1 and Table 1).

Table 1: Studies on esophageal achalasia and COVID-19.

Citation	Year of publication	Title	Country	Number of reported cases
Catillo et al ⁴⁰	2023	Acute respiratory failure secondary to megaesophagus: think beyond COVID-19	Mexico	1
Wasim et al ³⁹	2023	Acute-onset achalasia following a recent COVID-19 infection: a case report	Saudi Arabia	1
Zafra et al ¹⁵	2022	Infection with SARS-COV-2 as potential achalasia trigger	Spain	1
Mohammed et al ¹⁴	2022	Post-COVID-19 achalasia?	USA	1

Continued.

Citation	Year of publication	Title	Country	Number of reported cases
Aponte et al ¹⁰	2022	Long COVID-19 and achalasia: a possible relationship?	Venezuela	21
Furuzawa-Carballeda et al ¹²	2022	Is the SARS-CoV-2 virus a possible trigger agent for the development of achalasia?	Mexico	7
Zeidan et al ²	2022	A132 achalasia following a SARS-COV-2 infection: a case report	Canada	1
Cali et al ¹¹	2021	An unexpected thoracic finding in a patient with COVID-19	Italy	1
Gupta et al ¹³	2021	An interesting case of achalasia cardia with co-existing coronavirus 19 infection	India	1

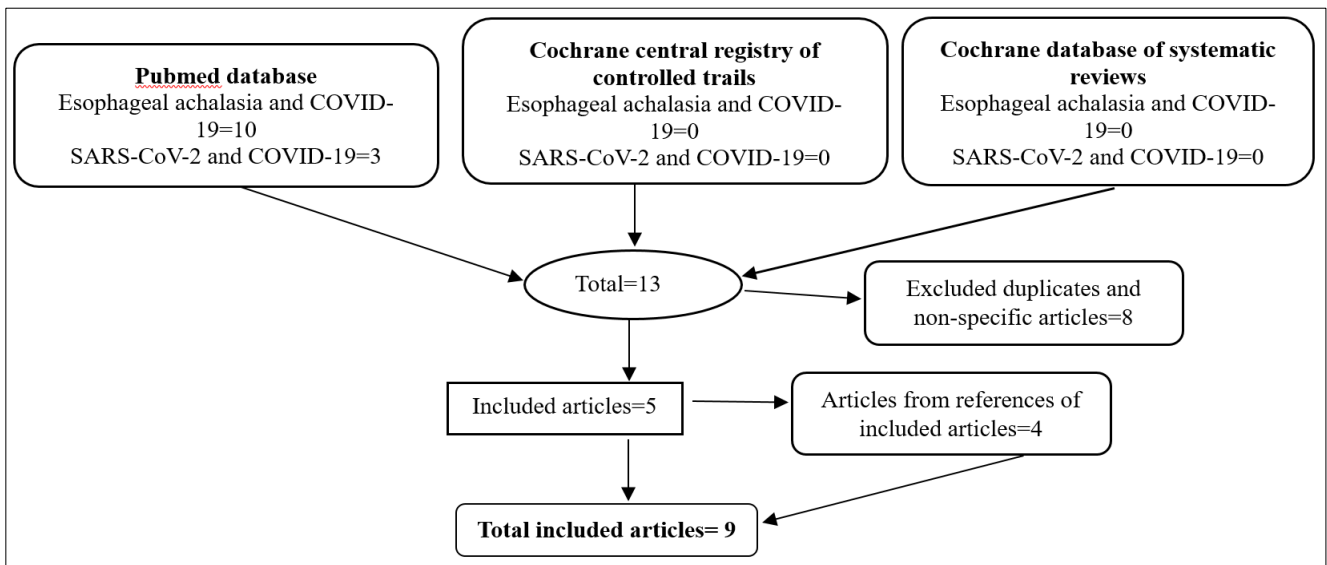


Figure 1: The flowchart of the study selection process.

Case report

A 9-month-old male child with isolated cleft of the soft palate was admitted to the pediatric surgical ward of the Obafemi Awolowo University Teaching Hospitals Complex for palatoplasty, in January 2021. He had hematological, and biochemical blood work up for surgery including a polymerase chain reaction (PCR) screening for COVID-19 which returned negative.

Palatoplasty was performed observing universal precaution and the surgical team was kitted with personal protective equipment (PPE). The patient underwent surgery under general anaesthesia and a Furlow’s double opposing Z-plasty was performed to repair the soft palatal cleft. However, the patient had repeated episodes of desaturation in the immediate postoperative period which necessitated re-intubation and eventual admission into the intensive care unit (ICU). Chest radiograph revealed bilateral pneumonic changes (Figure 2).

A repeat COVID-PCR for the child was requested and this returned a positive result. The patient’s mother also tested positively for COVID-19 after screening.



Figure 2: Chest radiograph showing bilateral pneumonic changes associated with COVID-19.

The child was mechanically ventilated and managed in the intensive care unit of OAUTHC. However, to prevent prolonged endotracheal intubation, a tracheostomy was done for the child. A repeat COVID-19 PCR test was done for the child, eleven days after the initial diagnosis, and it returned negative. Attempted decanulation resulted in desaturation and regurgitation of stale food. A computed tomography scan of the neck and chest was requested to

rule out subglottic stenosis. Computed tomography (CT) scan of the chest revealed a patulous esophagus, measuring about 27.5 mm in its widest diameter (Figure 3), but ruled out subglottic stenosis. The patient was thus referred to the cardiothoracic surgical team. Further investigation with a barium swallow revealed a moderately dilated thoracic esophagus with suggestions of persistent short segment abrupt change in caliber near the oesophagogastric junction at the T10 level (Figure 4). A diagnosis of mild severity childhood achalasia was made. Patient had laparotomy for modified Heller's myotomy under general anaesthesia and was discharged home.



Figure 3: Cervical computed tomography (CT) scan showing a patulous esophagus, measuring about 27.5 mm in its widest diameter.



Figure 4: Barium swallow showing a moderately dilated thoracic oesophagus with persistent short segment abrupt change in caliber near the oesophagogastric junction at the T10 level.

DISCUSSION

As the world marks the end of the COVID-19 pandemic, there is a growing need to understand its potential long-term consequences, especially those that manifest as post-infection complications.

This study aims to investigate an unusual but critical complication - esophageal achalasia, which, to date, has been reported in only a handful of cases following COVID-19 infection. Given the rarity of this association and its potential impact on individuals' health, it is essential to

explore the relationship between COVID-19 and achalasia further.

Achalasia is a motor disorder of the esophagus caused by reduction or loss of myenteric plexus neurons in the distal esophagus and lower esophageal sphincter (LES), leading to aperistalsis and failure of lower oesophageal sphincter relaxation.¹⁶ It is a rare but debilitating disorder of motility of the oesophagus characterized by the inability of the lower oesophageal sphincter (LES) to relax and allow the passage of foods and liquids.¹⁷ It affects approximately 0.3-1.3:100,000 individuals/year worldwide.⁹

The disease is characterized by aperistalsis, sub-optimal relaxation and an increase in the resting tone of the lower oesophageal sphincter during swallowing.¹⁸ Symptoms typically present in middle-aged individuals and include dysphagia to ingestion of solid and liquid foods, chest pain, regurgitation and weight loss.¹⁹ There is limited utility of physical examination in contributing to the diagnosis of esophageal achalasia, emphasizing the importance of employing specific diagnostic tools. Diagnosing achalasia involves a thoughtful approach utilizing imaging studies and ultimately esophageal manometric studies. In the absence of manometry, barium swallow is emerging as a crucial diagnostic tool.²⁰ The characteristic bird's beak appearance and esophageal dilatation revealed by this imaging technique provide valuable insights into the structural anomalies associated with achalasia.²¹ There are diverse management strategies aimed at alleviating symptoms and improving the quality of life for individuals with achalasia. Pharmacologic and non-surgical interventions, such as calcium channel blockers and nitrates, offer viable options, especially for elderly patients who may face limitations in undergoing more invasive procedures.²²

The utilization of endoscopic intra-sphincteric injection of botulinum toxin in specific cases further demonstrates the nuanced and patient-tailored nature of achalasia management.²³ Surgical interventions, including laparoscopic Heller myotomy with partial fundoplication and peroral endoscopic myotomy (POEM), represent more definitive approaches to address the underlying motility issues.²⁴ The consideration of endoscopic dilation as an initial step in cases where surgery may be less feasible underscores the importance of a step-wise and adaptive approach in managing this complex disorder.²⁵ In this article, barium swallow was used in aiding diagnosis highlighting the role of imaging studies in identifying this disease.

The aetiology of achalasia remains unclear and several pathologic mechanisms, including underlying viral infection, idiopathic autoimmune trigger, and genetic susceptibility, have been suggested as potential causes.⁵ Viral infections in particular have gained interest as a potential trigger for achalasia due to the presence of inflammation and viral particles found in the oesophageal tissue of achalasia patients.¹² More recently, research into

the association of SARS-COV-2 virus with achalasia has gained the attention of the scientific community with the occurrence of achalasia in patients that had COVID-19 infection. Although there are few reports of post-COVID-19 infection achalasia in the literature, to our knowledge, there has been no report of this case in a young child. Thus, this case report is the youngest case presentation in the literature.

Theories on the association between viral infection and achalasia have been postulated. One of such theories is that viral infection may lead to autoimmune response that damages the neurons in the oesophagus, resulting in the failure of the lower oesophageal sphincter (LES) to relax.²⁶ Another theory suggests that viral infection may lead to inflammation in the oesophagus which may disrupt the function of the neurons that control the LES.¹² There is also evidence to suggest that certain viruses may be more strongly associated with achalasia than others. Several patho-mechanisms, including underlying viral infection, idiopathic autoimmune trigger, and genetic susceptibility, have been suggested as potential causes.²⁶ These processes have been linked to immunologic and inflammatory reactions that ultimately lead to the destruction of the myenteric plexus in the lower oesophageal sphincter.²⁷

The association between viruses and achalasia was first suggested by the observation of viral particles in the oesophageal tissues of achalasia patients.²⁶ Previous studies have identified the presence of herpes simplex virus type 1 (HS-V 1) and cytomegalovirus in the oesophageal tissues of patients with achalasia.^{27,28} Subsequent studies have identified other viruses including human papillomavirus (HPV) and measles virus, in oesophageal tissues from achalasia patients.¹⁶ The Epstein-Barr virus (EBV), Varicella Zoster virus (VZV), human immunodeficiency virus (HIV) and Paramyxoviruses have also been linked to achalasia.²⁷ The presence of viral particles in the oesophageal tissues of achalasia patients suggests a potential role for viruses in the development of this disorder. The exact mechanism by which viruses may trigger achalasia is still unclear.²⁹ However, the presence of angiotensin-converting enzyme 2 (ACE-2) receptors in the gastrointestinal epithelium, including the oesophagus makes it susceptible to SARS-COV-2 infection.

The SARS-COV-2 virus belongs to the family betacoronavirus and is an enveloped, positive-sense, single-stranded RNA virus.³⁰ The membrane protein, envelope protein, and spike protein make up the coronavirus virion along with the nucleocapsid.³¹ The homotrimeric spike protein is required for viral particles to bind to and fuse with host cell membranes, which allows them to enter host cells.³² Once within the host cells, it proceeds through replication and maturation, which causes an inflammatory reaction by activating and invading immune cells with different cytokines.³³ SARS-COV-2 virus has an affinity for ACE-2 receptor.³⁴ It can bind to and infect human cells through this protein. The lungs, heart, arterial blood vessels, kidneys, liver, and

gastrointestinal system all contain these receptors.²⁸ ACE-2 is the SARS-COV-2's major receptor for cell entry.³⁵ These receptors aid the entry of SARS-CoV2 virus into the cells of the respiratory and gastro intestinal system.³²

Excitatory neurotransmitters like acetylcholine and inhibitory neurotransmitters like vasoactive intestinal and nitric oxide are involved in the complex mechanism of esophageal motility, which also involves extrinsic innervation and local reflex arcs.³⁶ In addition to these neurotransmitters, the distal oesophagus' angiotensin II receptor type II (ATR1 receptor), which is activated by the renin-angiotensin system (RAS) and angiotensin II (AII), serves as a potent activator of esophageal contractions.³⁷ Both the blood vessel walls of the lamina propria of the distal esophagus and the capillary walls at the tip of the papillae contain ACE.^{37,38}

This review amalgamates insights from various case reports and studies, shedding light on the complex relationship between COVID-19 and the development of achalasia. The case, reported by Cali et al, highlights the challenges in managing refractory achalasia, particularly in unique cases with complicating factors such as severe hypothyroidism and edentulous conditions.¹¹ The article underscores the importance of considering various therapeutic options, but in this case, per-oral endoscopic myotomy was not deemed suitable. This emphasizes the need for tailored approaches in managing achalasia based on individual patient characteristics. The study by Aponte et al also explores a potential relationship between long COVID-19 and achalasia, noting an increased frequency of achalasia cases during the years 2020 and 2021, with a significant proportion of these patients having a history of COVID-19 infection.¹⁰

The authors suggest a possible link between type II achalasia and COVID-19, implicating the ACE 2 receptor, which the SARS-COV-2 virus exploits to infect host cells. However, the study acknowledges the retrospective nature and calls for further research to validate this relationship. The case report presented by Wassim et al adds to the growing evidence of an association between COVID-19 and achalasia.³⁹ The reported acute-onset achalasia in a 38-year-old male following a recent COVID-19 infection raises questions about potential pathophysiological mechanisms. The authors suggest that COVID-19 may contribute to the development of achalasia, emphasizing the importance of considering esophageal complications in patients presenting with respiratory symptoms. Zafra et al in their study provides further support to the idea of SARS-COV-2 as a potential triggering agent for idiopathic achalasia.¹⁵

The case report of a 66-year-old male developing achalasia after a mild SARS-COV-2 infection aligns with the hypothesis that viral infections, including COVID-19, may induce a loss of esophageal neurons, leading to a likely irreversible motor disorder. The importance of tailoring treatment based on individual health status is emphasized,

acknowledging the complexity of managing post-COVID-19 achalasia. Gupta et al also reported a case of a 48 year old male with COVID-19 infection and achalasia.¹³

The correspondence letter by Mohammed and Krogel, titled "post-COVID 19 achalasia," adds weight to the emerging evidence of post-infectious gastrointestinal dysmotility after a COVID-19 infection.¹⁴ The presented case further contributes to the growing body of knowledge suggesting a potential relationship between COVID-19 and the development of achalasia. Furuzawa-Carballeda et al in their recent study reportedly detected the SARS CoV-2 virus in the lower oesophageal sphincter in six out of seven patients who had achalasia following COVID-19 infection.¹² ACE-2 receptor was also expressed in the lower esophageal sphincter of all the patients and controls.

In our case report, our patient had PCR COVID-19 screening 4 days prior to surgery. Our patient had an atypical presentation and did not present with the typical symptoms of dysphagia to ingestion of solid and liquid foods, chest pain, regurgitation, and weight loss.

Attempted decanulation of our patient resulted in regurgitation of stale food and subsequently oesophageal dilatation was discovered after a computed tomography scan of the chest. Other atypical presentation has also been reported by Castillo et al where they highlighted acute hypercapnic respiratory failure as a rare presentation of achalasia following a COVID-19 infection in a 61-year-old man.⁴⁰

CONCLUSION

In conclusion, we report a case of a child who was diagnosed with COVID-19 infection post palatoplasty and subsequently was diagnosed with achalasia. Our report highlights that the presentation may sometimes be atypical and clinicians should have a high index of suspicion to rule out achalasia in patients with a history of COVID-19 infection. We also recommended that patients who have a history of COVID-19 infection should undergo multidisciplinary assessments during the first and second year after discharge to rule out post infection complications of COVID-19. Investigations including barium swallow and/or computed tomography scan of the chest is recommended to screen for achalasia once clinical findings give an index of suspicion.⁴¹ The unexpected complication of esophageal achalasia post-COVID-19, as explored in the reviewed articles, warrants careful consideration in clinical practice. The interplay between viral infections, including COVID-19, and the development of achalasia is complex and multifaceted. Further research is imperative to elucidate the underlying mechanisms, validate the observed associations, and guide tailored therapeutic approaches for individuals facing the challenges of achalasia in the aftermath of COVID-19.

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