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Achalasia Following a SARS-CoV-2 Infection and Recent COVID-19 Immunization in a 20-year-old Female

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Abstract

Achalasia is an esophageal disorder characterized by loss of inhibitory neurons of the myenteric plexus in the lower esophageal sphincter, presenting with dysphagia, chest pain, and regurgitation. Although the etiology of achalasia is unknown, it has been associated with viral infections, and recent studies have noted concurrence of achalasia cases with COVID-19 infection. The case discussed in this report pertains to a 20-year-old female with a recent history of COVID-19 infection and subsequent SARS CoV-2 vaccine administration, presenting to the Emergency Department with a complaint of chest pain and shortness of breath. She was incidentally diagnosed with achalasia, after concern for pulmonary embolism prompted CT angiography of the chest. This case is unique due to the patient's young age and lack of confounding ongoing medical issues to consider when analyzing disease presentation, as well as its potential link to COVID-19 infection. We hypothesize that SARS-CoV-2 might have caused a deviant immune response in this patient, leading to vagus nerve damage and the development of achalasia. With this case report, we hope to further explore the connection between COVID-19 and achalasia to help guide clinicians to potential viral etiologies of achalasia, allowing them for a prompt and efficient diagnosis and patient management.

Keywords

Achalasia, SARS-CoV-2, COVID-19, Case Report

Abbreviations

LES: Lower Esophageal Sphincter; GI: Gastrointestinal; ED: Emergency Department; PE: Pulmonary Embolism; COVID-19: Coronavirus Disease 2019; SARS CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; CT: Computerized Tomography; ACE2: Angiotensin-Converting Enzyme-2; IV: Intravenous

Case Report

Introduction

Achalasia is a motor disorder of the esophagus which results from degeneration of myenteric plexus neurons in the distal esophageal wall. The progressive destruction of inhibitory ganglion cells leads to unmatched excitation and failure of the Lower Esophageal Sphincter (LES) to relax. Food in the esophagus is thus unable to pass into the stomach which results in esophageal dilatation. An absence of normal peristalsis might also be observed. Thus, it presents with dysphagia, food regurgitation, heartburn, and substernal chest pain [1].

Achalasia is an uncommon disorder with a prevalence of 10 cases per 100 000 inhabitants, and with an annual incidence of one new case per 100 000 inhabitants [1]. The etiology of primary or idiopathic achalasia is unknown; however, it has been shown that anti-myenteric neuronal antibodies are present in affected patients, which suggests an autoimmune process [2]. Some studies propose that the attack on esophageal neurons in achalasia is triggered by an immune response to viral infections (eg: herpes zoster, measles viruses) [3]. Specifically, it was proposed that the inflammatory response to viral infections, consisting of CD3/CD8-positive cytotoxic T lymphocytes, eosinophils, and mast cells, might lead to loss of myenteric plexus ganglion cells present in patients with achalasia [4]. Recent reports indicate a possible connection between the SARS-CoV-2 virus and achalasia [5-7]. Esophageal dysmotility is suspected to be part of the constellation of symptoms of dysautonomia in Long COVID-19 patients, hypothesized to be caused by vagus nerve fiber damage [8,9].

SARS-CoV-2 is a single stranded virus that is generally transmitted through respiratory droplets. Cases of fecal-oral transmission have been confirmed in the US, indicating that the virus can replicate in both respiratory and digestive tracts [10]. Once infected, an individual most commonly experiences respiratory, gastrointestinal (GI), and other symptoms. SARS-CoV-2 virus enters host cells through the angiotensin-converting enzyme-2 (ACE2) receptor, which is present on numerous cell types throughout the human body, including oral cavity, nasal cavity, lungs, esophageal epithelial cells, gastric glandular cells, enterocytes, etc. Consequently, ACE2 receptor expression can explain the multisystem organ involvement and great spectrum of symptoms COVID-19 infected patients experience. The GI symptoms result when SARS-CoV-2 enters enterocytes through ACE2. Once inside a cell, the virus replicates and causes an inflammatory cytokine response which mediates the various GI symptoms (**Fig-1**). These proinflammatory cytokines include IL-1, IL-6, IL-12, IFN-γ, and TNF-α [11]. In particular, IL-6 has been found to be elevated in patients with a worse prognosis and to contribute to a cytokine storm in such patients [11].

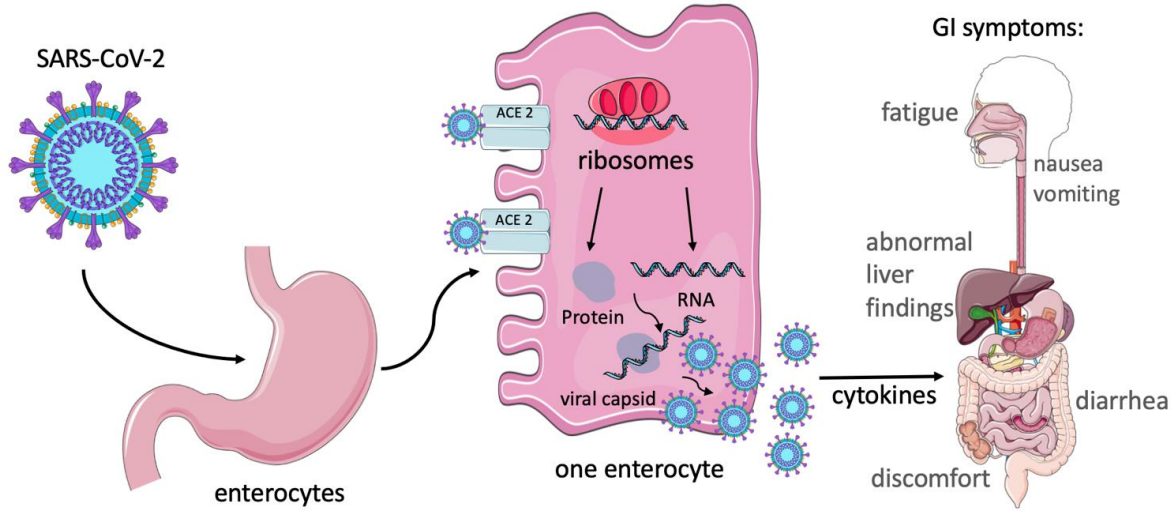

Fig-1: SARS-CoV-2 effect on enterocytes and resultant GI symptoms.

Case Report

The patient was a 20-year-old female with no significant past medical history who presented to the Emergency Department (ED) in distress, complaining of chest pain and shortness of breath. She was infected with SARS-CoV-2 a month prior to the ED encounter and received a COVID-19 vaccine one day prior to visit. The patient reported being on birth control medication and denied recent travel, including to South America. She reported experiencing shortness of breath but denied nausea/vomiting, headache, dizziness, and abdominal pain. She did not have any alteration of limb, bowel, or bladder function. The patient denied thoughts of self-harm and hallucinations. No additional information on the patient's past medical, family, and social history was declassified for use in this study.

On physical examination, the patient was alert and oriented with no difficulty breathing and speaking in full and complete sentences. Her heart rate was 90 beats per minute, respiratory rate was 17 breaths per minute, and oxygen saturation was 99%. She was afebrile at 36.8°C and her blood pressure was 112/66 mm Hg. The patient had no neurological deficits and displayed good strength with normal sensations. Her lungs were clear to auscultation, and the patient had no abdominal tenderness or pulsatile masses.

A complete blood count with differential, chemistry panel, thyroid stimulating hormone, troponin, d-dimer, and electrocardiogram were ordered. The findings of these tests were in normal limits, with the exception of a low lipase enzyme of 5 U/L and an elevated D dimer of 858 ng/mL.

A clinical suspicion and concern for pulmonary embolism (PE) was noted and so a computerized tomography (CT) angiography of the chest with contrast was ordered as well. Imaging revealed asymmetrically prominent left axillary lymph nodes and a dilated thin-walled esophagus with air fluid level near the gastroesophageal junction with an achalasia pattern (**Fig-2**). No filling defects were noted in the main, left, right, or lobar pulmonary arteries. There were no signs of effusion, pneumothorax, or lobar consolidation. Heart size was normal. No pericardial effusion and no evidence of mediastinal lymphadenopathy was present.

The history of presentation, physical examination, laboratory findings, and CT imaging were consistent with achalasia. The administered treatment included Motrin, Intravenous (IV) fluids, and IV Protonix. Observations in the ED showed improvement. After discussing with the gastroenterology physician on-call, the patient was discharged and recommended to take Protonix orally as well as advised to avoid solids with follow-up in an outpatient clinic for completion of esophageal manometry test and pneumatic dilation intervention.

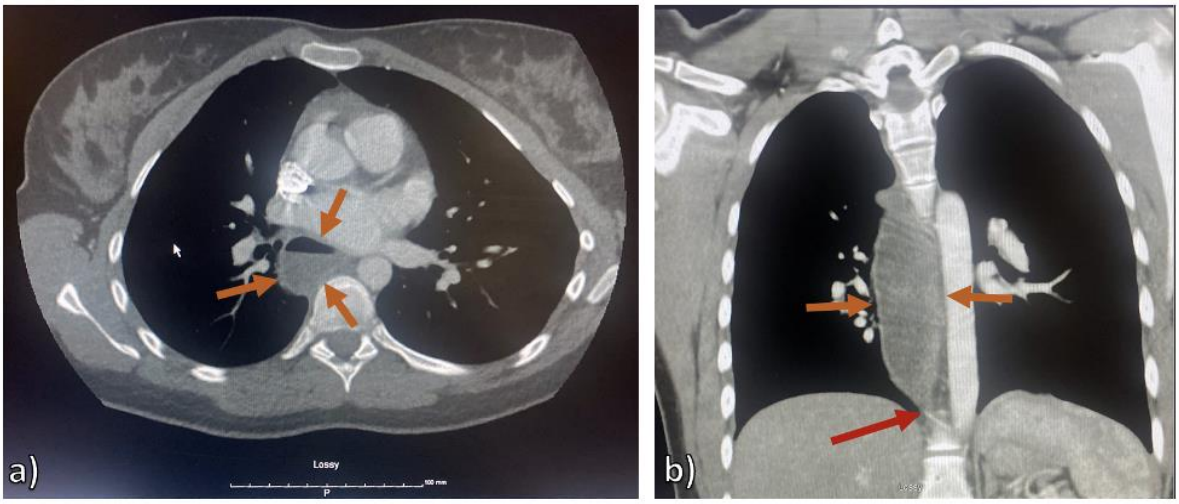

Fig-2:

CT angiogram of chest with contrast (a) transaxial and (b) coronal planes with the arrow pointing to the tortuous and markedly dilated thin-walled esophagus (orange arrows), which smoothly tapers to a beak at the gastroesophageal junction (red arrow). On the transaxial view, residual food debris and air are present in the dilated esophagus (orange arrows).

Discussion

The patient's chest pain and shortness of breath are non-specific symptoms prompting consideration of broad as well as possible life-threatening differentials. Chest pain is one of the known symptoms of achalasia, but it could also be attributed by the patient's distress and/or the side effects of the SARS-CoV-2 vaccine administered the day prior to the visit. Her shortness of breath instigated evaluation of the pulmonary arteries for PE; however, rather than pulmonary artery filling defects, CT angiography revealed a dilated thin-walled esophagus. With suspicion of achalasia, CT imaging and barium swallow x-ray can be done to look for the characteristic "bird's beak" appearance caused by increased LES resting pressure [12].

The patient was also found to have an elevated D-Dimer. A hypercoagulable state caused by the patient's stated use of birth control remains a probable cause of the elevated D-Dimer [13]. Another potential cause is the patient's recent SARS-CoV-2 infection. Recent studies suggest that the pathogenesis of hypercoagulability caused by SARS-CoV-2 infection is due to the spike protein activating the alternative complement pathway, as well as activating C5b-9 complement proteins [14]. Despite the infection occurring a month prior, studies show that up to 39% of patients suffer from persistent "COVID symptoms" four weeks after infection [15].

The patient workup also showed low serum level of lipase, which can be seen in advanced chronic pancreatitis associated with alcohol/tobacco abuse. Given that the patient was a previously healthy young woman with no abdominal pain and no signs of substance abuse, this diagnosis is unlikely. Research has suggested the involvement of SARS-CoV-2 infection with pancreatic damage, as recent studies have shown ACE2 receptors present in pancreatic tissue [16]. However, in these cases serum levels of lipase were elevated, making this unlikely to be the cause of low lipase in this patient.

Ultimately, the patient's non-specific clinical presentation and chemistry findings were inconclusive, and diagnosis of achalasia could not have been made on these factors alone. CT angiography and clinical correlation of symptoms were imperative to ascertain the most likely cause of the patient's distress. The patient's observed improvement of symptoms with Motrin, IV fluids, and IV Protonix is a promising indication that the diagnosis of achalasia was correct. However, esophageal manometry is required to establish the diagnosis [12]. The specific manometric findings of achalasia are incomplete relaxation of the LES and aperistalsis in the distal two-thirds of the esophagus. Thus, further investigation in a gastroenterology clinic and completion of manometry, upper GI endoscopy, and pneumatic dilation are necessary for confirmation of the diagnosis.

Our assessment of patient presentation together with recent published studies [5] and case reports [6, 7] on the topic support the hypothesis that there might be a causal link between COVID-19 infection and development of achalasia. Although the mechanism of SARS-CoV-2 gastrointestinal manifestations is unknown, the presence of ACE2 receptors in the esophagus may serve as a viral target site, causing an inflammatory cytokine response which leads to the degeneration of the inhibitory neurons in the myenteric plexus responsible for the achalasia. Furthermore, recent studies have shown a link between vagus nerve fiber damage and patients with severe COVID-19 infection [8], which can be correlated with observed Wallerian degeneration in vagal fibers found in some patients with achalasia [9]. A recent report strengthens the hypothesis, finding that at 8 weeks post recovery from COVID-19 infection, 8% of patients presented with unexplained dysphagia [17]. Another study establishes epidemiologic support for the connection by revealing that the prevalence of achalasia at their clinic increase in 2021 as compared to 2016-2019 and that 67.86% of their patients treated for achalasia showed either clinical or molecular evidence of COVID-19 infection [5].

Conclusion

This case provides a useful look at a patient presenting with chest pain in the ED following a COVID-19 infection and a subsequent SARS-CoV-2 vaccine administration, who was ultimately diagnosed with achalasia. The patient was a 20-year-old female with no significant medical history; thus, there was little to no potential confounding ongoing medical issues to consider when analyzing disease presentation

and its potential link to COVID-19 infection. We hope that this report inspires further investigation into the association between viral infections such as COVID-19 and achalasia. With improved understanding of the etiology of achalasia, clinical diagnosis and treatment may be better guided and nutritional consequences minimized.

Conflict of Interests

All authors declare that they have no conflicts of interest to disclose in this case report.

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