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Hypoxic respiratory failure in acute appendicitis: A bronchoperitoneal fistula as the presenting symptom of appendicitis in the setting of pediatric COVID-19

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ABSTRACT

Symptomatic COVID-19 less frequently affects the pediatric population and is often associated with atypical presenting symptoms. Here we describe a nine-year-old patient who presented with acute hypoxic respiratory failure and was found to have perforated appendicitis, intra-abdominal abscess, and bronchoperitoneal fistula. The rapid progression of this pathology, complex critical care decision making, and ultimate surgical management has not been previously described. Documenting this patient's clinical course and effective treatments may serve to inform and guide the medical community and pediatric care providers as the world continues to combat the COVID-19 pandemic.

1. Introduction

Appendicitis is the most common surgical issue in the pediatric population. It presents in 19–28 per 10,000 children younger than the age of 14 [1] and is diagnosed in 1 in 8 children evaluated urgently for abdominal pain [2]. The classic findings of periumbilical pain migrating to the abdominal right lower quadrant (RLQ), anorexia, nausea, and signs of localized or generalized peritonitis are less common in school age children than in adults. In school age children from the age of 5–12, the most prevalent finding is RLQ tenderness (82%), followed by nausea (79%) [3]. The most common complication of acute appendicitis is perforation, and the rate of perforated appendicitis decreases with age starting as high as 83% in neonates [4] and decreasing to 11 to 32% in children aged 5 to 12 [5]. Atypical presentations of appendicitis include appendicitis occurring in inguinal [6] and femoral [7] hernias, intussusception of the appendix [8], and appendicitis causing scrotal abscesses [9]. Rarer still is the development of a bronchoperitoneal fistula after perforated appendicitis. A PubMed search of bronchoperitoneal fistula resulted in only 6 unique case reports and only one case in 1947 that was secondary to appendicitis [10]. We therefore present this very rare patient case as it has not been described in the literature for about 75 years.

2. Case description

The patient is a 9-year-old Hispanic male who presented to a local emergency room with the chief complaint of difficulty breathing.

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The patient and family are Spanish-speaking thus history was acquired with assistance from an interpreter. The patient had a two-day history of coughing and decreased energy. On the evening of presentation, he had an episode of emesis with coughing. He ambulated with assistance into the ER and initial vitals revealed an oxygen saturation of 70%, heart rate of 170, temperature of 101.8 F, respiratory rate in the 40s, and a normotensive blood pressure. The patient was immediately started on supplemental oxygen, received a DuoNeb treatment, IV steroids, and IV fluid bolus. A rapid COVID-19 test was performed and resulted negative. A chest x-ray and noncontrast CT of the chest, abdomen, and pelvis were completed which showed evidence of a subphrenic abscess that had necessitated through the diaphragm into the pleural space, and signs of perforated appendicitis (Fig. 1, Fig. 2). The patient's respiratory status continued to worsen, and he was emergently transferred to our tertiary care children's hospital via air transport.

On arrival to our facility, the patient was critically ill, distressed, hypotensive on a continuous dopamine infusion, and oxygen saturations were as low as 8–30% despite use of supplemental oxygen and non-rebreather mask. He was intubated and started on an epinephrine drip. The chest X-ray revealed a large right pneumothorax in the subpulmonic area (Fig. 1); thus, a right pigtail chest tube was placed with immediate purulent output and continuous air leak. Saturations slowly improved; however, the patient remained persistently hypoxic, with saturations not rising above 70%. The decision was made to undergo Venous-Venous Extra Corporeal Membrane Oxygenation (VV ECMO) cannulation with a 27 French Avalon catheter in the right internal jugular. Placement was performed under direct ultrasound imaging, and once in appropriate position, patient was heparinized and VV ECMO initiated, with near immediate improvement in oxygen saturation to above 90%. The post-operative chest x-ray demonstrated the catheter in good position (Fig. 3).

Continuous Renal Replacement Therapy was initiated through the ECMO circuit and the patient was started on Total Parenteral Nutrition (TPN). The patient tested positive for COVID-19. He received convalescent plasma, IVIG, and completed a ten day course of Remdesivir and extended course of methylprednisolone. He also tested positive for adenovirus and rhino/enterovirus.

Enteral feeds were started when his hemodynamic status improved, and he was quickly advanced to full enteral nutrition. The patient underwent successful ECMO decannulation on post-operative day eight. His pigtail chest tube remained in place with purulent drain output and persistent air leak. The patient's hospital course was complicated by pulmonary emboli and the persistence of an air and fluid collection (Fig. 4). Repeat imaging demonstrated an extension of a fluid and air collection from the right lower abdominal quadrant through the diaphragm and into the pleural space, consistent with a bronchoperitoneal fistula.

The patient was transitioned to an oscillator to promote healing of the bronchoperitoneal fistula and underwent CT-guided drain placement by the Interventional Radiology team for peri-appendiceal abscess secondary to perforated appendicitis. Post-procedure the patient's condition acutely worsened. Additional imaging revealed communication between the drain and colonic lumen (Fig. 5).

The patient accumulated additional intraperitoneal air, and the decision was made to proceed to the operating room for diagnostic laparoscopy and definitive drainage. In the operating room, a dime sized hole in the right hemidiaphragm was noted anteriorly, close to the midclavicular line. Pulmonary parenchyma was visually identified beyond this defect and when saline was placed in this area an active air leak was identified. Due to the chronicity of this fistula, the area was drained with a 8.5 French Fuhrman pigtail tube and a 15 French Blake drain. The remainder of the abdomen was surveyed and a walled off peri-appendiceal infectious process was noted and not disturbed. With proper drainage, the patient began to slowly recover. His course was complicated by Drug Rash with Eosinophilia

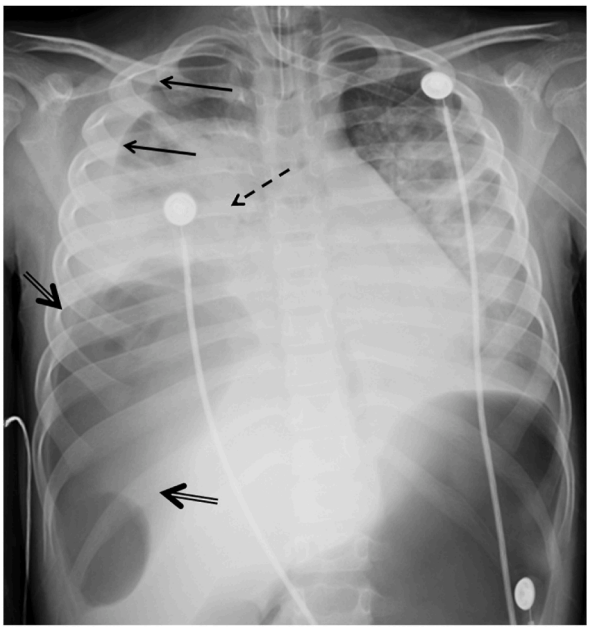

Fig. 1. Frontal supine portable radiograph of the chest shows large right pleural effusion layering to the apex (black arrows), consolidation of the lower lobes (black dashed arrows) with silhouetting of the right hemidiaphgram, and large collection of air at the interface of the right hemidiaphgram and right lower chest (black double arrow).

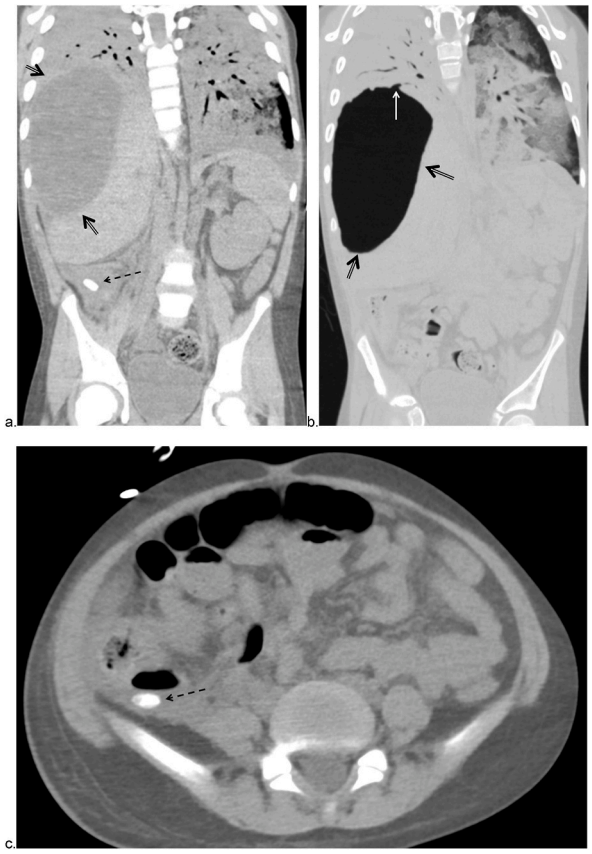

Fig. 2. Noncontrast CT of the chest and abdomen. **2a.** Coronal image shows a large hypoattenuating subphrenic fluid collection that effaces the liver and elevates the right hemidiaphragm (black double arrow) and calcified appendicolith in the right lower quadrant (black dashed arrow). **2b.** Coronal image at a slightly more anterior location shows air within the subphrenic collection communicating with a right lower lobe segmental airway (white arrow). There is consolidation of the lower lobes with air bronchograms, and patchy groundglass opacities in the periphery of the left lung, characteristic of covid pneumonia. **2c.** Axial view of the calcified appendicolith (black dashed arrow), which is extraluminal and within an air-fluid collection, indicative of perforated appendicitis.

and Systemic Symptoms (DRESS) syndrome, thus patient remained on high doses of steroids. He underwent tracheostomy before discharge (Fig. 6).

At his follow-up clinic appointment, two months post-hospital discharge, the patient was recovering well. The patient and his mother denied any new complaints and stated he had been regaining weight. He had completed his steroid taper and had his tracheostomy tube downsized. He did not have any shortness of breath or difficulty breathing at rest. A Chest Xray was acquired which revealed continued asymmetric elevation of the right hemidiaphragm, but overall improved expansion of both lungs since his inpatient stay. The film revealed a mild chronic interstitial prominence centrally, with no pneumothorax. The patient will require an interval appendectomy for his perforated appendix, and the plan is for continued rehabilitation and appendectomy in four to six months.

3. Discussion

This is an interesting case study on the management of complicated appendicitis and bronchoperitoneal fistula, superimposed with acute COVID-19 infection. Diagnosis of this unique pathology was made using CT imaging. Early CT in this patient was crucial for identification of the life-threatening bronchoperitoneal fistula. CT is limited in the visualization of the diaphragm itself, thus in differentiating fluid or air in the subpulmonic versus subphrenic spaces; however, in coordination with clinical interventions, such as the initial drain placement, it became apparent that a connection from the bronchiole to the pleural space, through the diaphragm and into the peritoneum existed.

The patient described here is of Hispanic ethnicity and his family did not speak English. In a study using the 2009 Kid's Inpatient Database, of the 96,865 pediatric patients with appendicitis, perforation at presentation was more common among Hispanics compared to Caucasians (32.5% vs 23.9%, $p < 0.001$). Hispanic pediatric patients were more likely to have a complication (OR 1.123, $p = 0.001$), and had a longer length of stay in the hospital by 0.73 more days (3.07 days vs 2.34 days, $p < 0.001$) [11]. A similar study with 89,935 pediatric patients with appendicitis found being Hispanic had an odds-ratio for complicated appendicitis of 1.07 (CI 1.03–1.11, $p < 0.001$) compared to being Caucasian. Interestingly, being transferred from an acute care hospital had an increased risk of complicated appendicitis (OR 1.39 CI 1.32–1.47, $p < 0.001$) as did being at a dedicated Children's Hospital (OR 1.70 CI 1.64–1.77, p

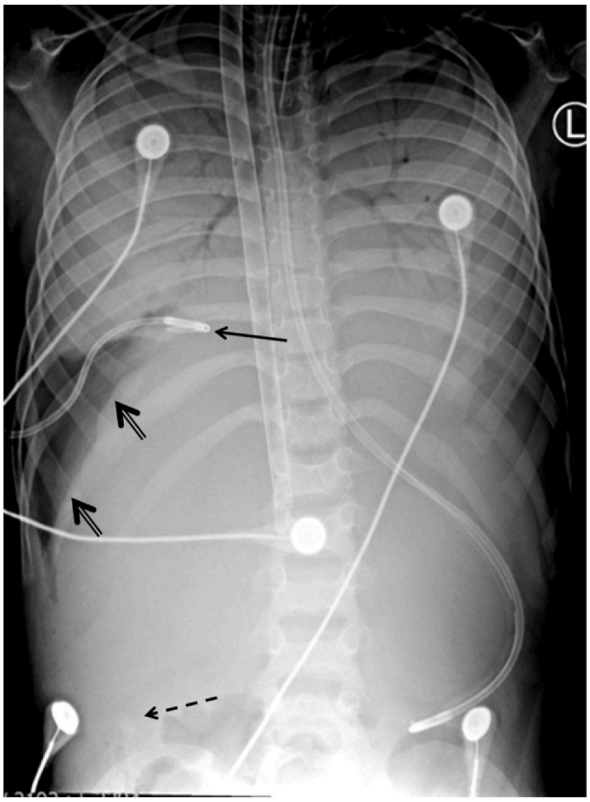

Fig. 3. Frontal supine portable chest radiograph shows the venovenous ECMO cannula, right pigtail chest tube (black arrow) and reduced size of the subphrenic air-fluid collection (black double arrows) and appendicolith in the right lower quadrant (black dashed arrow).

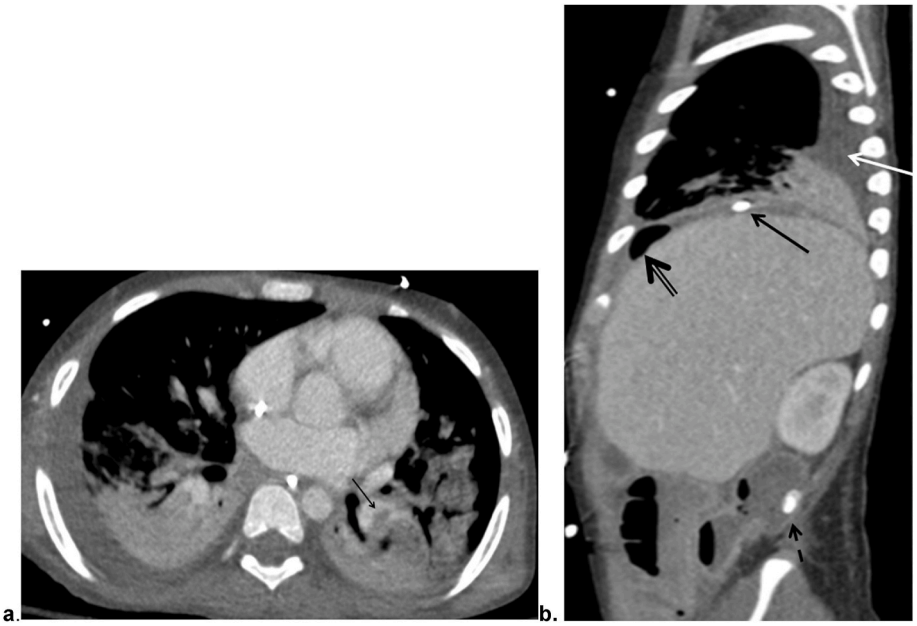

Fig. 4. 4a. Axial image from CT pulmonary angiogram shows filling defects in lower lobe segmental pulmonary arterial filling defects representing pulmonary emboli (black arrow). **4b.** Sagittal CT image shows small subprhenic air-fluid collection (double black arrow) containing the tip of the pigtail drainage catheter (black arrow), appendicolith within extraluminal fluid collection (dashed black arrow), small pleural effusion (white arrow). Bibasilar consolidations also present.

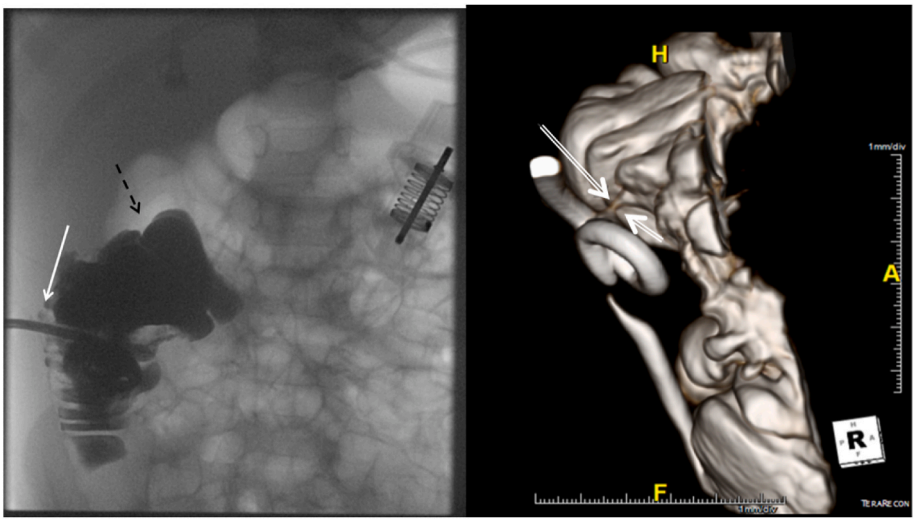

Fig. 5. Fluoroscopic supine frontal image of the right hemiabdomen obtained during contrast injection of pigtail drainage catheter (white arrow = catheter). Contrast fills the colonic lumen (dashed arrow) and a small fistula between the peritoneum and colonic lumen are noted on subsequent oblique CT 3D surface rendering of the contrast (double white arrow).

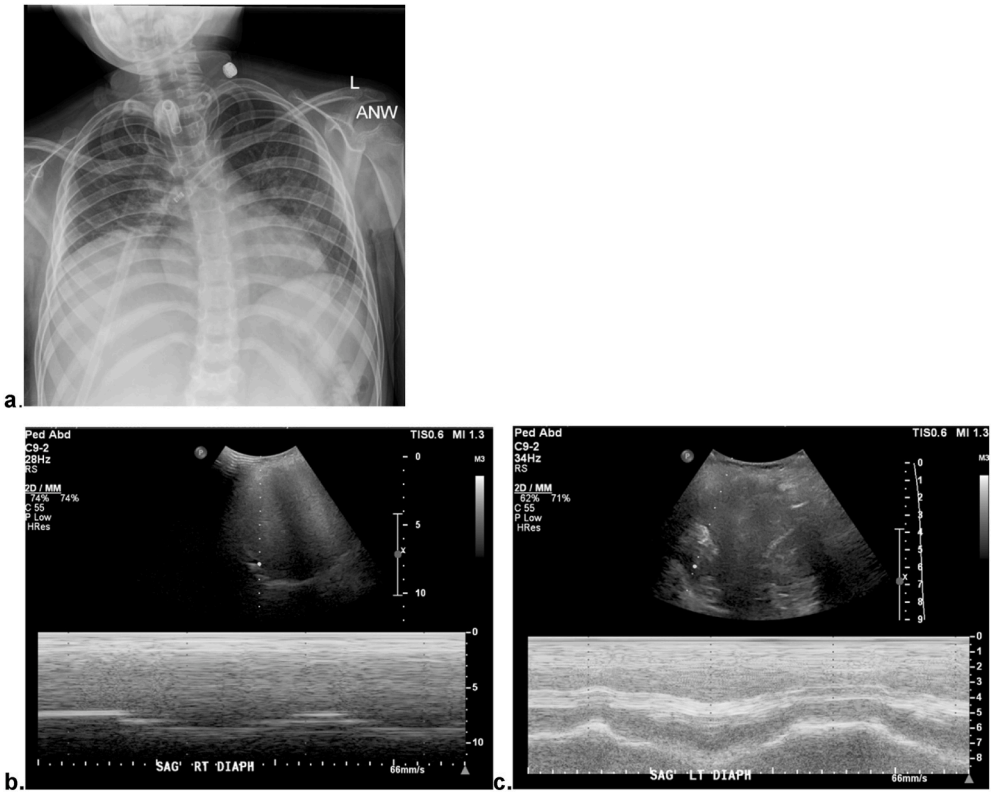

Fig. 6. Chest X-ray on day of discharge shows tracheostomy tube tip at the midthoracic trachea and elevated right hemidiaphragm. **6b,c.** M-mode sonographic images show reduced excursion of the right hemidiaphragm (2 cm), compared to the normal left side (3–4 cm).

< 0.001) [12]. Another prospective, cross-sectional study of 10 pediatric emergency departments with 1001 pediatric patients with appendicitis found that the risk of perforated appendicitis was even higher among Hispanic patients with limited English proficiency. Additionally, this study showed non-English speaking Hispanics (OR 0.77 CI 0.59–1.00) were less likely to receive advanced imaging [13].

This patient's clinical course was further complicated by the presence of COVID-19. Since first presenting in late 2019, the

collective understanding of the presentation of COVID-19, especially in the pediatric population, has been rapidly evolving. In the United States, children account for approximately 14% of COVID-19 cases [14] of which approximately one third are asymptomatic [15]. In children age 0 to 9 the most common symptom was fever (46%), followed by cough (37%) and diarrhea (15%) [16]. The full spectrum of COVID-19 presentations and complications is wide and continues to be studied. Beyond presenting symptoms, the rapid and accurate detection of COVID-19 has also been an area of urgent public health research and clinical need. In this case, the patient had a negative rapid test at his initial presentation, however on repeat testing, proved positive for COVID-19.

Given the high prevalence of both appendicitis and COVID-19, there is a substantial overlap of patients who have both. A retrospective study at a single location noted a temporal relationship between a peak in COVID-19 cases in their area and increases in cases of acute appendicitis. This could possibly suggest that appendicitis is associated with a post-infectious hyper-inflammatory state of COVID-19 [17]. Another retrospective review examined a total of 196 CT images during the peak of COVID-19 from March 2020 to May 2020 compared to 2019 and found that fewer patients presented for appendicitis (55 in 2020 vs 141 in 2019); however, a higher proportion of patients were found to have appendicitis (46% in 2020 vs 30% in 2019, $p = 0.038$), and a higher proportion demonstrated severe appendicitis (92% in 2020 vs 57% in 2019, $p = 0.03$) [18]. These findings were reproduced and reiterated by other studies which also revealed a longer symptom duration prior to presenting to the ED, higher rates of complicated appendicitis, longer length of hospital stay, and longer duration of symptoms compared to prior to the COVID-19 pandemic [19–22].

This case was a rare presentation of a perforated appendicitis complicated by a bronchoperitoneal fistula. Previously, the literature has reported cases of bronchoperitoneal or broncho-abdominal fistulas from subphrenic abscesses including as a sequela of appendicitis [23], cholecystectomy [24], colorectal anastomotic leak [25], gastric leak status post laparoscopic sleeve gastrectomy [26], and as a sequela of retained drains [27]. In each case, the presence of an intra-abdominal collection eroded through the diaphragm and eventually though the pleura and into an airway. Although there were several reports of subphrenic abscesses and bronchoperitoneal fistulas in the early 1900s, such reports have become exceedingly rare in the contemporary literature. This is likely due to the advent and popularization of antibiotics. A variety of surgical procedures such as thoracoplasty, muscle flaps, and decortication have been used in the past to treat bronchoperitoneal fistulas, but recently there has been a trend toward non-operative management and use of chest tubes, drains, and conventional and high frequency ventilation [28]. The general principles behind the management of these fistulas are to remove or control the provoking source and to reduce the pressure gradient in order to promote healing. In the setting of the patient's COVID-19 infection and bronchoperitoneal fistula, he was not able to adequately oxygenate and required VV ECMO. This had the added benefit of allowing the team to use rest ventilator settings in order to reduce the pressure gradient and promote fistula healing. After ECMO decannulation, the patient was transitioned to high frequency oscillatory ventilation.

Since first being used in the 1970s, ECMO has seen significant improvement in outcomes. In the pediatric population, 72% survive to decannulation from pulmonary support 60% survive to discharge from the hospital [29]. The first randomized control trial in 1994 comparing survival of ECMO patients ($n = 19$) compared to patients who were conventionally ventilated ($n = 21$) did not show any benefit with an overall survival rate of 33% in ECMO vs 42% in mechanical ventilation ($p = 0.08$) [30]. A subsequent randomized control trial in 2009 of 180 patients did however show a survival benefit with ECMO. In this study, 90 patients were randomized to be considered for ECMO at an institution with high case volume versus 90 patients treated with conventional methods. Of the 90 patients considered for ECMO, 68 (75%) received ECMO and this randomized group had a 63% survival at 6 months compared to 47% survival for the conventional group ($RR = 0.69$, $p = 0.03$) [31]. After this study, there was a rapid increase in the number of ECMO centers with the 115 centers in 1998 growing to 164 centers in 2009, and now 492 centers by 2020 [29]. By the time COVID-19 emerged, benefits and safety of ECMO had been well-documented. COVID-19 created a greater demand for ECMO as the patients refractory to conventional treatments for Acute Respiratory Distress Syndrome (ARDS) increased dramatically. Registry data and retrospective studies among COVID-19 patients on ECMO for pulmonary support showed that the survival rate was greater than 60% and in line with survival statistics among ECMO patients for other disease processes [32,33]. In this case, we believed the patient to have a reversible process along with a good long-term prognosis and was therefore a reasonable candidate for ECMO. We encourage similar patients to be considered for ECMO therapy.

4. Conclusion

This rare case highlights the need for a higher suspicion for atypical presenting symptoms of COVID-19 and appendicitis in the pediatric, and especially Hispanic pediatric population. There is a high value of CT imaging in this group when the patient is stabilized. ECMO should be considered at ECMO centers when patients display refractory potentially reversible acute respiratory failure. Swift escalations in therapy and a multidisciplinary critical care team were necessary to stabilize and rescue this patient from the rapid clinical decline seen with this pathophysiology. Finally, despite the presence of an appendicolith, interval appendectomy is most appropriate for the critically ill patient recovering from acute hypoxic respiratory failure requiring VV ECMO.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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