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Acute appendicitis presenting with MIS-C secondary to COVID-19

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ABSTRACT

Acute Appendicitis (AA) is among the most common causes of abdominal pain in children. Several physical exam findings, scoring systems, and imaging studies, such as ultrasonography and computed tomography, exist to assist clinicians in diagnosing acute appendicitis. Despite multiple tools for assessing suspected acute appendicitis, it remains a challenge to diagnose acute appendicitis in the pediatric population. A challenge that becomes increasingly more difficult if presenting with a comorbid condition. With the emergence of coronavirus disease 2019 (COVID-19) and subsequent discovery of multisystem inflammatory syndrome in children (MIS-C), this case series presents three pediatric cases of acute appendicitis presenting concurrently with MIS-C secondary to prior COVID-19 infection thus illustrating potential complications to diagnosing and managing acute appendicitis.

1. Introduction

Acute appendicitis (AA) is among the most common causes of acute abdominal pain in children, with slightly greater lifetime risk for males, 8.6% compared to 6.7% for females [1]. Appendicitis is believed to be caused by obstruction of the appendiceal lumen, thereby allowing bacterial overgrowth [2]. Lymphoid hyperplasia frequently serves as the etiology of appendiceal obstruction and has been associated with various inflammatory conditions such as respiratory infections, measles, and mononucleosis [1]. Positive findings that help to confirm AA in pediatric patients are decreased or absent bowel sounds, positive psoas sign, positive obturator sign, and positive Rovsing's sign [2]. Several scoring systems also exist, including the Alvarado Score, the Pediatric Appendicitis Score, and the Appendicitis Inflammatory Response Score, which can assist clinicians in determining the likelihood of acute appendicitis [3]. Furthermore, diagnosis is aided by Ultrasonography (US) and Computed Tomography (CT), with the former preferred as the initial diagnostic imaging in the pediatric population [2]. Despite these methods, AA remains a challenge to diagnose in the pediatric population, a task that becomes increasingly more difficult if presenting with a comorbid condition. This case series presents three pediatric cases of AA presenting concurrently with Multisystem Inflammatory Syndrome in Children (MIS-C) secondary to prior Coronavirus Disease 2019 (COVID-19) infection which were seen and treated at a suburban community hospital that offers inpatient pediatric services.

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2. Case series

2.1. Case 1

A 16-year-old male with no past medical history presented to the emergency department (ED) with sore throat, subjective fever, and abdominal pain. Five days prior to admission he developed abdominal discomfort, subjective fevers, and non-bloody and non-bilious emesis. The last emesis was one day prior to admission. Due to worsening abdominal pain, which had localized to the epigastrium and the right lower quadrant, he presented to our ED.

In the ED, vitals showed fever of 102.6 Fahrenheit (F), tachycardia at 118, normotension at 128/67, and normal oxygen saturation on room air. On exam, the patient had a systolic murmur and guarding on abdominal palpation with positive McBurney's point. Evaluation was significant for complete blood count (CBC) with no leukocytosis, white blood cell count (WBC) was 12 with a neutrophil predominance 83.1%, mild normocytic anemia with hemoglobin/hematocrit (H/H) of 12.8/38.9, and normal platelets 219. Erythrocyte sedimentation rate (ESR) was elevated at 21 and C-reactive protein (CRP) was elevated at 5.8. Complete metabolic panel (CMP) was significant for mild hyponatremia at 134 and mild hyperglycemia of 123. Electrocardiogram (EKG) showed abnormal ST elevation in isolated leads. Echocardiogram was normal. Chest X-Ray (CXR) showed no acute cardiopulmonary disease. US of the abdomen showed a 6mm appendix with minimal free fluid. CT scan of the abdomen/pelvis with contrast was inconclusive due to lack of oral contrast in the colon, although it did note mesenteric adenitis. The patient was admitted to the inpatient pediatric service for observation and started on intravenous fluids (IVF), piperacillin-tazobactam, and pain control.

Throughout the night, the patient continued to experience worsening abdominal pain. The following morning, a repeat US of the abdomen showed a 9mm appendix with minimal free fluid and continued RLQ mesenteric adenitis. Rapid COVID-19 was negative and CRP up-trended to 14.7. In the evening on day one of hospitalization, he was taken to the operating room (OR) for laparoscopic appendectomy where the appendix was found to be severely inflamed with phlegmon. Intravenous (IV) metronidazole was started.

On post-operative day (POD) one, he was upgraded to the pediatric intensive care unit (PICU) as he continued with fevers, tachycardia, and borderline hypotension with associated exam findings of ill-appearance, delayed capillary refill, and murmur at the left lower sternal border. Labs showed thrombocytopenia at 120, elevated liver function tests (LFT), and elevated CRP at 19.0. Piperacillin-tazobactam was switched to meropenem and metronidazole was continued. On POD two, the patient developed worsening hypotension despite IVF boluses and labs showed up-trending CRP at 19.7, worsening thrombocytopenia at 83, and hypoalbuminemia 2.3. A right subclavian central line was placed at bedside, and he was started on a dopamine drip and albumin. He also developed respiratory distress requiring Bilevel Positive Airway Pressure (BiPAP) to maintain oxygen saturations. CXR showed increasing bilateral infiltrates, so he was started on furosemide. On POD three the patient remained febrile with an up trending CRP at 25.8 and thrombocytopenia at 71. Repeat CXR showed persistent bilateral infiltrates. Norepinephrine was started to maintain blood pressure and fluconazole was added for empiric coverage.

On POD four, the CRP up trended to 26.7, which represented an atypical post-operative finding suggesting the potential for an alternative process activating the inflammatory pathway. Evaluation for Multisystem Inflammatory Syndrome in Children (MIS-C) secondary to prior COVID-19 infection was initiated. Evaluation showed elevated procalcitonin at 2.19, elevated D-Dimer at 972, elevated prothrombin time (PT) at 17.9, elevated partial thromboplastin time (PTT) at 46.4, elevated troponin at 0.193, and elevated brain natriuretic peptide (BNP) at 11,100. Fibrinogen and ferritin were within normal limits. COVID-19 PCR, COVID-19 IgM, and COVID-19 IgG were collected. Repeat echocardiogram showed mildly elevated right ventricular systolic pressures according to the tricuspid jet insufficiency with normal function. Due to concern of MIS-C secondary to COVID-19, the patient was started on intravenous immunoglobulin (IVIG) and steroids. Dopamine was weaned off.

On POD five, he was afebrile for more than 48 hours. Labs showed thrombocytopenia at 109, CRP down-trended to 23.4, D-Dimer up-trended to 1375, troponin down-trended to 0.060, and negative COVID-19 PCR. Norepinephrine was weaned off and fluconazole was discontinued. Anti-coagulation was held in the setting of thrombocytopenia. On POD six, the thrombocytopenia resolved as platelets increased to 198. Other labs included CRP down-trending at 7.5, down-trending BNP at 2020, normal PT at 12.8, normal PTT at 33.7, elevated D-Dimer 1375, and elevated troponin at 0.037. COVID-19 IgM was negative. Enoxaparin was started for deep vein thrombosis (DVT) prophylaxis in the setting of elevated D-Dimer and resolved thrombocytopenia. On POD seven, the CRP and D-Dimer continued to down-trend. COVID-19 IgG resulted positive, thus confirming the diagnosis of MIS-C secondary to prior COVID-19 infection. Repeat CT scan of the abdomen/pelvis showed bilateral atelectasis, small bilateral effusions, and small free fluid in the pelvis, which was attributed to postoperative changes. On POD nine, the patient continued to improve. Troponin was normal and CRP down trended to 1.7. Methylprednisolone was switched to every 24 h to start corticosteroid wean.

By POD eleven, the patient was downgraded to the inpatient pediatric service. D-Dimer spiked again to 1628 but a repeat the same evening was 830. On POD thirteen, the patient remained stable with a normal CRP and BNP. However, D-Dimer remained elevated at 671. A repeat echocardiogram was normal, showing no increased systolic pressures. The patient was discharged home with baby aspirin, prednisolone, and amoxicillin-clavulanic acid with outpatient follow-up with the pediatrician, pediatric general surgery, and pediatric cardiology.

2.2. Case 2

A 10-year-old male with past medical history of asthma, anaphylactic peanut allergy, and migraines presented to the ED for abdominal pain. Five days prior to admission, he developed abdominal pain and fever, with temperature max (T-max) of 104.9 F. Two days prior to admission, he presented to the ED for the same complaints. Vitals showed fever of 100.9 F, tachycardia at 152, respiratory rate at 16, hypertension at 136/77, and normal oxygen saturation of 98% on room air. Physical exam was significant for a well appearing, anxious male with minimal erythema of the left tympanic membrane without purulence or bulging, mild tenderness across

the upper abdomen without rebound or guarding, and non-tender McBurney's point. Evaluation was significant for CBC with leukocytosis, WBC was 16.6 with a neutrophil predominance at 80.4%, H/H at 14.0/40.4, and normal platelets at 323. CRP was elevated at 6.3. CMP was unremarkable. Urinalysis was significant for proteinuria at 30, ketonuria at 20, and moderate blood. Rapid COVID-19 antigen was negative. Blood culture was ordered and was negative. The patient received ceftriaxone 1000mg IV, ketorolac 15mg IV, and normal saline (NS) 1000ml IV bolus. The patient improved clinically and was discharged home from the ED with strict return precautions.

On the day of admission, the abdominal pain had localized to the right lower quadrant. Mother denied recent fever and review of systems was otherwise negative. Physical exam was significant for an uncomfortable but nontoxic male with right lower quadrant tenderness and positive McBurney's point without rebound tenderness. Evaluation was significant for CBC with no leukocytosis, WBC was 9.1 with continued neutrophil predominance, H/H of 12.9/38.3, and normal platelets at 286. The CRP up-trended to 7.8. CMP was unremarkable. Troponin was mildly elevated at 0.02, PT was elevated at 14.4, international normalized ratio (INR) was normal at 1.3, and PTT was normal at 28.1. Urinalysis was significant for proteinuria at 100, ketonuria at 5, and small blood. Repeat Rapid COVID-19 antigen was negative. CXR showed no evidence of any acute cardiopulmonary process. US of the appendix was suspicious for developing AA, with a noncompressible 6.5mm appendix, a small amount of fluid in the right lower quadrant, and multiple mesenteric lymph nodes, the largest measuring 9mm. Patient was started on piperacillin-tazobactam. Pediatric general surgery was consulted and laparoscopic appendectomy was performed that day without complication. Surgical pathology showed findings consistent with mild AA, including rare neutrophils within the appendiceal epithelium, and congested blood vessels in the serosa. The patient was admitted to the inpatient pediatric service that evening in stable condition. Discharge was pending return to normal diet and return of voiding and stooling.

On POD zero, the patient was intermittently febrile, with T-max of 102.7 F. Fevers resolved for approximately 8 h. However, on POD one, the fevers returned, with T-max of 103.1 F, and were accompanied by multiple episodes of watery, green diarrhea. Ibuprofen, acetaminophen, and cooling measures were ordered and IVF were continued due to poor oral intake, tachycardia, and diarrhea. On POD two, fever, with T-max of 103.1 F, and watery diarrhea persisted. COVID-19 PCR was ordered and was negative. The patient started culturelle and stool culture, stool ova and parasites (O&P), and *Clostridium difficile* (*C. difficile*) culture were ordered.

On POD three, the *C. difficile* culture was positive, so the piperacillin-tazobactam was discontinued and the patient was started on oral metronidazole and piperacillin-tazobactam was discontinued. Mother, who reported a history of antiphospholipid syndrome, noted she had had *C. difficile* multiple times, with her earliest episode at age seven and most recent episode several years ago. Physical exam showed the patient had cracked lips and mild conjunctivitis despite intravenous hydration and improved oral intake. Further questioning revealed that the patient had mild nasal congestion for approximately 24 h approximately six weeks prior to this admission for AA. MIS-C evaluation was immediately initiated. Evaluation showed elevated CRP at 19.6, elevated D-Dimer at 942, elevated PT at 15.8, elevated fibrinogen at 913, elevated troponin at 0.065, and elevated BNP at 20,100. EKG showed sinus tachycardia with nonspecific T wave abnormality. Echocardiogram showed a systolic function that subjectively appeared to be at the lower limits of normal with an estimated ejection fraction (EF) of 50%. CXR and US of the abdomen showed no acute abnormalities. The patient was started on IVIG at 85g, methylprednisolone 1mg/kg IV twice daily, aspirin 81 mg by mouth (PO) daily, and enoxaparin 65mg subcutaneous (SQ) daily. COVID-19 IgM and IgG were ordered and IgG was positive, consistent with the mother's report of prior illness and with the diagnosis of MIS-C secondary to prior COVID-19 infection.

On POD four, repeat laboratory studies were improved except for the D-Dimer which up-trended to 1239 and for mild thrombocytosis at 499. On POD five, the patient continued to improve clinically and the MIS-C laboratory studies were down-trending. Repeat echocardiogram showed improving ventricular ejection fraction at 60%. On POD seven, further history was elicited from the mother which revealed that in addition to the mother's history of antiphospholipid syndrome, the patient's maternal grandfather also had antiphospholipid syndrome, factor V leiden, and factor C deficiency which resulted in multiple episodes of DVT and pulmonary embolisms (PE) requiring daily anti-coagulation until he died from sudden cardiac death. Factor VII level was ordered inpatient, with the remaining thrombophilia evaluation planned outpatient.

On POD eight, repeat MIS-C laboratory evaluation showed up-trending D-Dimer at 1749 (compared to 906 on POD six). CBC showed steadily increasing thrombocytosis at 724 but normal WBC at 13.3 and H/H at 13.6/41.0. PT was normalizing at 13.8, INR was normal at 1.2, PTT was down-trending at 30.4, fibrinogen normalized at 420, and ferritin normalized at 294. BNP continued down-trending at 1090 and CRP was also down-trending at 2.3. CMP was remarkable for mild elevated glucose at 112, possibly secondary to steroid administration. Anti-Xa factor level was 0.53, which was elevated for prophylactic dosing, so the enoxaparin was decreased to 50mg SQ every 24 h. The patient remained hospitalized pending improvement of the D-Dimer and BNP. On POD nine, the D-Dimer continued to trend upward at 1782. Factor VII level was low at 42. Upon extensive discussion with the patient and mother regarding remaining hospitalized for continued trending of the D-Dimer, the family preferred to discharge home on enoxaparin with close hematology follow-up of the D-Dimer. At discharge, the methylprednisolone taper was continued at 1mg/kg PO daily for five days, then tapered to 0.5mg/kg PO for five days, and then discontinued. The patient was also discharged on enoxaparin 40mg SQ once daily for DVT prophylaxis, aspirin 81 mg PO daily, and metronidazole 400mg PO three times daily for eight days. He was discharged home with outpatient follow-up with the pediatrician, with pediatric hematology for D-Dimer monitoring and thrombophilia evaluation including factor V leiden, protein C antigen and function, and antiphospholipid antibodies, with pediatric cardiology for repeat echocardiogram, and with pediatric general surgery.

2.3. Case 3

A 5-year-11-month old male with no significant past medical history presented as a transfer from an outside facility for fever and abdominal pain which was believed to be secondary to severe ileus versus small bowel obstruction (SBO). The patient complained of a

twelve day history of abdominal pain and fever. Fever occurred daily, with a T-max of 102.4 F orally, and was relieved with acetaminophen. The patient complained of generalized abdominal pain which was worse with movement and better with leaning forward. Seven days prior to admission, the patient went to urgent care where kidney-ureters-bladder X-Ray (KUB) showed constipation. The patient was discharged home with glycerin suppository and polyethylene glycol. The abdominal pain continued, so he presented to our facility later that same day where COVID-19 testing was performed and he was ultimately discharged home. Five days prior to admission, he developed nausea and vomiting and presented to an outside facility where he was given ondansetron IV and an IVF bolus before being discharged home. Two days prior to admission, he developed loose, non-bloody diarrhea and continued with intermittent nausea and vomiting. On the day of admission, he complained of fever, abdominal pain, nausea, vomiting, and bilateral hip pain. Of note, one week prior to admission both parents tested positive for COVID-19.

At the outside ED, the evaluation was significant for CBC with leukocytosis, WBC was 18.4, CMP with mild hyponatremia at 132 and mild hypokalemia at 3.3, and PT elevated at 13.5. INR and PTT were normal. Influenza, Respiratory Syncytial Virus, and Streptococcus swabs were negative. Urinalysis was significant for ketonuria at 80, proteinuria at 30, and moderate bacteria. CXR was negative. KUB showed prominence of multiple loops of small bowel and colon, nonspecific however consistent with diffuse bowel ileus. Non-contrast CT scan of the abdomen/pelvis showed multiple dilated loops of small bowel throughout the abdomen up to 3cm with air fluid levels concerning for bowel obstruction, differential included severe bowel ileus; mild right hydronephrosis was also noted. He received ceftriaxone once, morphine once, ondansetron once, and NS 500ml IV bolus, and was transferred to our facility for pediatric general surgery evaluation.

On admitting physical exam, the patient was ill-appearing but nontoxic with legs held in bilateral flexion secondary to abdominal pain, bowel sounds were appreciated, diffuse abdominal tenderness with gentle palpation, non-distended, no guarding, no rebound, not tympanic, otherwise exam was unremarkable. Chart review on admission, showed the COVID-19 test performed one week prior was positive. The patient was admitted to the inpatient pediatric service with the diagnoses of abdominal pain (severe ileus vs SBO), COVID-19 positive (rule out MIS-C), elevated D-Dimer, hyponatremia, and right hydronephrosis. Nasogastric tube (NGT) was placed and set to low intermittent suction. Pediatric general surgery was consulted, MIS-C evaluation was initiated, stool studies were ordered, and analgesics were ordered (avoiding opioids). On admission, evaluation was significant for CBC with leukocytosis, WBC was 20.4, stable H/H, and thrombocytosis at 485. CMP showed mild hyponatremia at 134 and low bicarbonate at 17. MIS-C work-up showed elevated CRP at 14.1, elevated ESR at 41, elevated D-Dimer at 4125, mildly elevated PT at 12.8, normal INR, low PTT at 21.6, normal troponin at <0.012, mildly elevated BNP at 143, and mildly elevated triglycerides at 91. Ferritin at 190, fibrinogen at 467, and lactic acid at 0.8 were all within normal limits. Given the elevated D-Dimer, the patient was started on enoxaparin for DVT prophylaxis.

On the night of admission, the NGT was dislodged but the patient remained stable and abdominal X-Ray was unchanged with or without the NGT, so it was not replaced. On day one of admission, the patient continued with diffuse abdominal pain, but the pain was localizing more to the right lower quadrant. Repeat labs showed CBC with improving leukocytosis, unremarkable CMP, elevated PT at 15.7, normalized PTT at 27.3, down-trending D-Dimer at 2628, and down-trending CRP at 13.6. SBO was ruled out after a small bowel series demonstrated slow progression of contrast through the bowel. Echocardiogram was read as normal. US of the abdomen was performed and the appendix was not visualized. Piperacillin-tazobactam was started but steroids were held. Peripherally inserted central catheter (PICC) consent was obtained but ultimately the PICC was never placed. The patient started peripheral parenteral nutrition (PPN). Given the laboratory findings and his clinical picture, IVIG and low dose aspirin were started for concern of MIS-C secondary to COVID-19 infection. COVID-19 IgM and IgG were ordered.

On day two of admission, the patient continued with abdominal pain. Labs showed up-trending thrombocytosis at 502 but down-trending CRP at 5.6. EKG showed normal sinus rhythm. US of the appendix showed an 8.7mm appendix with appendicolith, consistent with AA. He was diagnosed with AA but due to other coexisting conditions causing overall poor condition, it was recommended that he continue nonsurgical management by continuing piperacillin-tazobactam IV and starting metronidazole IV. He continued PPN as he advanced to a clear liquid diet (CLD). Ketorolac was started as the acetaminophen was no longer helping with his pain. On day three of admission, the abdominal pain was improving with the ketorolac. The patient complained of one loose, non-bloody bowel movement but he was ambulating to the couch thereby showing an improved activity level. Repeat labs showed CBC with down-trending thrombocytosis at 476, down-trending D-Dimer at 1006, and stable CRP at 5.6. The patient was tolerating diet, so PPN was discontinued as he was advanced to a regular pediatric diet.

On day four, the abdominal pain was improving, and he continued to tolerate regular diet, however, the patient continued to complain of loose stools. On physical exam, he was comfortable at rest but had right lower quadrant tenderness, without guarding or distention. Laboratory studies showed up-trending ESR at 71, down-trending CRP at 3.5, up-trending D-Dimer at 1470, and negative EBV. CT scan of the abdomen/pelvis demonstrated peripherally enhancing collections of the right lower quadrant (RLQ), possibly a single collection with two components, measuring 3.3×2.8 cm and 5.5×2.2 cm, which may be abscess formation; no evidence of hydronephrosis was noted. Piperacillin-tazobactam and metronidazole IV were continued. The patient was made nothing by mouth (NPO) at midnight for possible drain placement with Interventional Radiology (IR). On day five of hospitalization, the patient continued to complain of abdominal pain and noted red tinged stool, but no gross blood. Labs showed up-trending D-Dimer at 4283, normal repeat troponin at < 0.012, normal BNP at 87, and positive repeat COVID-19 PCR. Ultimately, the patient was improving on IV antibiotics, so percutaneous drains were not placed for the intra-abdominal collections and he resumed a regular diet.

On day six, the patient continued to clinically improve. Repeat labs showed thrombocytosis at 462, down-trending D-Dimer at 910, hypoalbuminemia at 3.0, down-trending CRP at 1.6, negative COVID-19 IgM, and positive COVID-19 IgG. MIS-C secondary to prior COVID-19 infection was confirmed with positive COVID-19 IgG antibodies despite continued positive COVID-19 PCR. The patient continued aspirin, enoxaparin, famotidine, piperacillin-tazobactam, and metronidazole. As the patient continued to improve on IV antibiotics, the plan was for interval appendectomy in approximately 6–8 weeks. By day seven, the abdominal pain had resolved. His

Table 1
Comparison of laboratory data and imaging for the patient Cases.

	16 year old	10 year old	5 year and 11 month old
Vitals (temperature, HR, RR, BP, and oxygen saturation)	99.0 F, 118, 20, 128/67, and 99% on room air	98.5 F, 120, 20, 135/85, and 100% on room air	97.7 F, 114, 22, 123/80, and 97 % on room air
CBC (WBC, H/H, and Plt count)	12.0k with neutrophilia 83.1k, 12.8/38.9, and 219k	9.1k with neutrophilia 73.7%, no bandemia, 12.9/38.3, and 286k	20.4k with neutrophils 55%, bandemia 25%, 12.0/35.5, and 485k.
BMP (Na, K, Cl, CO2, BUN, creatinine, and glucose)	134, 4.3, 99, 26, 9, 0.71, and 123	138, 3.8, 102, 25, 11, 0.48, and 110	134, 3.6, 103, 17, 9, <0.40, and 90
AST/ALT	52/31 CMP was on day 2	38/24	46/8
TBili, indirect and direct billirubin	T Billi 0.8 CMP was on day 2	0.6, 0.5, and 0.0	T. Billi 0.4
Total protein and albumin	5.2/2.3 CMP was on day 2	8.0/4.2	6.2/2.8
CRP	5.8	7.8	14.1
PT/INR and APTT	17.9/1.6 and 46.4	14.4/1.3 and 28.1	12.8/1/1 and 21.6
D-Dimer	972	942	4125
Fibrinogen	419	913	467
Troponin	0.193	0.065 elevated	<0.012
BNP	11100	20100	143
SARS-CoV-2 IgG Antibody (ELISA)	Positive	Positive	Positive
SARS-CoV-2 Antigen (Rapid)	Negative	Negative	Not performed
SARS-CoV-2 IgM Antibody (ELISA)	Negative	Not performed	Negative
SARS-CoV-2 PCR	Negative X 2	Negative	Positive
Appendix Ultrasound	Linear structure probably appendix measuring 6mm and normal caliber, and minimal free fluid	Appendix 6.5 cm, non-compressible, echogenic mesenteric fat, no appendicolith, small amount of free fluid RLQ, and mesenteric lymph nodes with largest 9mm.	Appendix is not well seen, free fluid in RLQ, and dilated bowel loops in RLQ.
Chest x-ray	No acute cardiopulmonary disease	No acute cardiopulmonary disease	Not performed
POC troponin	Not performed	0.02	Not performed
ESR	21	Not performed	41
Lactic Acid	1.3	Not performed	0.8
EKG	Normal sinus rhythm and nonspecific ST changes	Sinus tachycardia, nonspecific T wave abnormality	Normal sinus rhythm
ECHO	Unremarkable	Cardiac function lower limit of normal	Unremarkable
Interleukin-6	Not performed	Not performed	38.6 (elevated)
Procalcitonin	2.19	Not performed	Not performed

Comparison table of laboratory values and imaging studies performed on each patient. Red indicates the laboratory values or images that were not done on admission, but throughout the course of the hospitalization. Note: Please use color for this figure.

stool was non-bloody and more formed and his oral intake neared baseline. On exam, normal bowel sounds and minimal RLQ tenderness were appreciated, otherwise his exam was normal. Labs were significant for down-trending D-Dimer at 744. He completed the course of piperacillin-tazobactam IV and transitioned to amoxicillin-clavulanic acid PO but required one more day of metronidazole IV. Enoxaparin was discontinued. On day eight of hospitalization, he completed the course of metronidazole IV. He was discharged home with aspirin, amoxicillin-clavulanic acid PO, and metronidazole PO with outpatient follow-up with the pediatrician, pediatric general surgery, pediatric hematology, pediatric nephrology, and pediatric cardiology.

Following discharge, the patient was followed by pediatric general surgery. He continued to complain of intermittent abdominal pain at his outpatient follow-up and was scheduled for interval laparoscopic appendectomy. Approximately two months after initial hospitalization, the patient underwent laparoscopic appendectomy. Intraoperative findings were significant for extensive inflammation, adhesions, and scarring of the appendix and RLQ, with the appendix being stuck in a retrocecal position in the RLQ. Pathology was performed and read as "a vermiform appendix measuring 3.7 cm in length and varies in diameter from 4mm distally to 9mm proximally; lumen is patent and filled with solid brown fecal material." Given the extensive adhesions involving the appendix and RLQ and ongoing intermittent abdominal pain following medical management, the prior diagnosis of acute appendicitis with abscess was confirmed.

3. Discussion

Fast and accurate diagnosis of AA reduces morbidity and mortality [2]. However, diagnosis of AA in pediatric patients remains a challenge as the younger patients demonstrate nonspecific symptoms which overlap with other diagnoses, may be unable to properly express their symptoms, and are more difficult to examine than older children and adults [1]. As a result, most patients less than five years old present late in the disease course thereby increasing their risk of complications such as abscess and perforation [1]. The emergence of COVID-19 and its association with MIS-C has further complicated the diagnosis and management of AA. According to the Centers for Disease Control, MIS-C causes systemic inflammation and may present with fever, abdominal pain, vomiting, diarrhea, neck pain, rash, bloodshot eyes, and fatigue [4]. Many of these symptoms overlap with those associated with AA which may delay the diagnosis of either condition if occurring concomitantly. Although more research is needed, it is possible that in these cases the appendix is obstructing secondary to systemic inflammation involving the gastrointestinal tract either by severe ileus, lymphoid hyperplasia, or some combination of both, as has been seen in other inflammatory conditions [1]. Conversely, MIS-C must also be kept on the list of differential diagnoses of children with complicated post-operative appendectomy courses which are not consistent with the expected post-operative complications and no source of bacterial sepsis can be identified. Table 1 outlines the common laboratory and imaging studies found in the patients described in this case series for reference.

4. Conclusion

In conclusion, this case series presents three pediatric patients whose hospital courses were complicated by concurrent AA and MIS-C secondary to prior COVID-19 infection, thus demonstrating a need for high clinical suspicion of both processes occurring simultaneously in any pediatric patient with abdominal pain to facilitate decreased morbidity and mortality through quick recognition and management of these potentially life-threatening conditions.

Patient consent

Written consent to publish this case report was obtained for all patients. However, this report does not contain any personal information that could lead to the identification of the patients.

Authorship

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

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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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