Acute abdomen in COVID-19 disease: the pediatric surgeon's standpoint

C. Rico Espiñeira, H. Souto Romero, R. Espinosa Góngora, M.L. Espinoza Vega, J.L. Alonso Calderón

Pediatric Surgery Department. Niño Jesús Pediatric University Hospital. Madrid (Spain).

ABSTRACT

Objective. To describe our experience in the diagnostic and therapeutic management of patients with acute abdomen as the main manifestation of SARS-CoV-2 infection.

Materials and methods. A descriptive study of patients with clinical signs of acute abdomen diagnosed with COVID-19 and admitted at out healthcare facility from April 1 to May 10, 2020 was carried out. Clinical records were reviewed for data collection purposes.

Results. A series of 14 patients (9 male and 5 female) with a median age of 9.5 years was analyzed. All patients had abdominal pain. There were 11 patients with fever, 9 patients with vomit or diarrhea, and 9 patients with clinically suspected surgical pathology (acute appendicitis or peritonitis). Increased acute phase reactants and coagulation disorders were a common characteristic at blood tests. An abdominal ultrasonography was carried out in all patients, and a CT-scan was performed in 4 patients, which demonstrated inflammatory signs in the terminal ileum, the ileocecal valve and the ascending colon, as well as gallbladder edema. Conservative management was decided upon in all patients except one, and eight patients required intensive care admission for support treatment.

Conclusions. Gastrointestinal symptoms can be the primary manifestation of the new coronavirus infection, which simulates an acute abdomen with a potentially unfavorable evolution. For an accurate diagnosis to be achieved, a good clinical record and a comprehensive physical exploration, as well as complementary tests in search of characteristic findings of COVID-19, should be carried out.

KEY WORDS: Abdominal pain; COVID-19; Acute abdomen; Pediatric surgery; Childhood.

ABDOMEN AGUDO EN LA ENFERMEDAD COVID-19. EL PUNTO DE VISTA DEL CIRUJANO PEDIÁTRICO

RESUMEN

Objetivos. Describir nuestra experiencia en el manejo diagnóstico y terapéutico de los pacientes que han presentado abdomen agudo como principal manifestación de la infección por SARS-Cov-2.

Material y métodos. Estudio descriptivo de los pacientes ingresados con clínica inicial de abdomen agudo que fueron diagnosticados de COVID-19 entre el 1 de abril y el 10 de mayo de 2020. Se ha realizado la revisión de historias clínicas para la recogida de datos.

Resultados. Describimos una serie de 14 pacientes (9 varones y 5 mujeres) con una mediana de edad de 9,5 años. Todos ellos consultaron por dolor abdominal acompañado de fiebre en 11 y vómitos o diarrea en 9, y la sospecha clínica inicial fue de patología quirúrgica (apendicitis aguda o peritonitis) en 9. En la analítica sanguínea se encontró como característica común elevación de reactantes de fase aguda y alteraciones de coagulación. Se realizó ecografía abdominal a todos los pacientes y tomografía computarizada en cuatro observándose signos inflamatorios en íleon terminal, válvula ileocecal, colon ascendente y edema de vesícula biliar. Se optó por un manejo conservador en todos los pacientes menos uno y ocho pacientes precisaron ingreso en cuidados intensivos para tratamiento de soporte.

Conclusiones. La infección por el nuevo coronavirus puede producir síntomas gastrointestinales como principal manifestación, simulando un abdomen agudo que en algunos casos puede evolucionar de forma desfavorable. Para el diagnóstico es preciso realizar una buena historia clínica y exploración física, así como pruebas complementarias en busca de hallazgos característicos de COVID-19.

PALABRAS CLAVE: Dolor abdominal; COVID-19; Abdomen agudo; Cirugía pediátrica; Infancia.

INTRODUCTION

On March 11, 2020, the World's Health Organization (WHO) declared the COVID-19 disease caused by the new SARS-CoV-2 coronavirus a pandemic. The region of Madrid was one of the most severely impacted in Spain. The strategic plan that came into force on March 21 cen-

Corresponding author: Dra. Clara Rico Espiñeira.
E-mail address: c.ricoesp@gmail.com

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Table I. Clinical characteristics of patients in chronological order of admission.

Patient	*Sex*	*Age (years)*	*Abdominal pain*	*Digestive symptoms*	*Other symptoms*	*Cutaneous involvement*	*Temp (°C)*	*HR (bpm)*	*BP (mmHg)*
1	M	12	Widespread	Vomit and diarrhea	Conjunctivitis	None	37.4	138	88/44
2	F	14	Widespread	Vomit	–	None	36.5	116	66/43
3	M	12	Widespread	Vomit and diarrhea	–	Petechiae	37.0	134	80/50
4	M	9	RIF	Vomit	Dysuria	None	36.3	117	81/47
5	M	10	Widespread	Vomit and diarrhea	Coughing and myalgia	Macular rash	35.6	118	80/40
6	M	13	RIF	Vomit	Dysuria	Macular rash	37.7	122	75/37
7	F	9	Widespread	Vomit and diarrhea	Coughing	None	36.6	130	104/65
8	F	2	RIF	Vomit	–	None	36.7	101	98/66
9	M	4	Hypogastrium and RIF	–	–	None	37.8	148	109/61
10	M	7	Periumbilical and RIF	Diarrhea	Coughing	None	38.0	125	94/36
11	M	8	Widespread	Diarrhea	Coughing and myalgia	None	37.7	109	95/58
12	M	12	RIF	Hyporexia	–	None	36.4	90	96/46
13	F	6	RIF	Vomit	–	None	39.1	146	104/66
14	F	15	Widespread	Diarrhea	Thoracic pain	None	37.1	96	116/61

M: male; F: female; RIF: right iliac fossa; Temp: temperature; HR: heart rate; BPM: beats per minute; BP: blood pressure. Altered levels: temperature >37.5°C, heart rate >110 bpm, BP <5th percentile for patient age.

tralized pediatric care within two regional hospitals, which meant our healthcare facility had to cover all pediatric pathologies requiring hospitalization or intensive care in an area that is usually served by 11 hospitals. This led to a significant increase in the number of surgical emergencies, especially acute abdomen patients requiring pediatric surgery department assessment. In this group of patients, various atypical cases with clinical signs compatible with acute abdomen or abdominal sepsis were found. Following complementary tests and evolution monitoring, they turned out to be COVID-19 cases. The objective of this study was to describe our experience in the diagnostic and therapeutic management of these cases in order to adequately identify them and avoid unnecessary surgeries, which could increase patient morbidity.

MATERIALS AND METHODS

An observational, retrospective study was carried out from April 1 to May 10, 2020. Patients under 18 years of age with clinically suspected acute abdomen diagnosed with COVID-19 at any stage and admitted at our healthcare facility (including those referred from other hospitals) were included. COVID-19 microbiological diagnosis was achieved using a polymerase chain reaction (PCRc19) test to detect the presence of SARS-CoV-2 in a nasopharyngeal swab sample, and also by means of serological techniques to detect blood antibodies. Patients diagnosed with COVID- 19 with digestive symptoms but without an abdominal exploration suggestive of acute abdomen, as well as patients with another etiologic cause for abdominal clinical signs, were excluded.

Demographic data, personal and contact history, clinical data, vital signs, radiological findings, and laboratory and microbiological results were collected by reviewing clinical records using the electronic clinical record system from our healthcare facility. Patient anonymity was preserved by numbering them in chronologic order of admission. Patient follow-up after discharge was conducted by the pediatrics department over the phone.

RESULTS

A series of 14 patients with a median age of 9.5 years (SD: 3.8) and without significant medical history was analyzed. The epidemiological survey carried out at anamnesis demonstrated a COVID-19 suspicious epidemiological environment in 3 patients, and contacts with confirmed cases in other 3 patients.

In all cases, the reason for consultation at the emergency department was abdominal pain, which had been present for 8 hours-5 days (mean: 1.78 days), and mostly associated with fever (11/14), vomit (9/14), and diarrhea (7/14). Fewer cases were associated with non-digestive symptoms, such as coughing, dysuria, myalgia, and thoracic pain (Table I).

Table II. Complementary test results.

Patient	*Lk x 1,000/µl*	*Nt x 1,000/µl*	*Ly x 1,000/µl*	*CRP mg/dl*	*Pct ng/ml*	*PI %*	*Fibrinogen mg/dl*	*D-Dimer mg/L*	*Ferritin ng/m*	*IL-6 pg/ml*	*PCRc19*	*Serology*
1	11.41	10.51	0.32	21.5	4.28	58	551	3.85	242	–	Positive	–
2	30.0	27.1	1.82	21.13	14.18	115	256	–	–	–	Negative	Positive
3	5.55	5.03	0.2	40.12	35.75	57	491	5.71	–	–	Positive	–
4	6.94	6.2	0.35	38.26	2.69	74	361	5.53	243	–	Negative	Positive
5	6.11	4.8	0.91	13.1	2.68	75	545	2.76	177	147	Negative	Positive
6	2.33	1.88	0.34	9.07	54.96	45	486	38714	188	–	Negative	Positive
7	7.33	6.43	0.42	24.84	1.84	73	532	2.26	–	96	Positive	–
8	13.85	10.79	2.22	16.97	0.83	79	550	–	–	–	Negative	Negative
9	16.2	12.4	2.21	26.14	18	55	612	0.88	147	44	Negative	Negative
10	10.62	8.63	1.04	4.2	0.88	–	–	1.31	–	–	Negative	–
11	15.19	10.6	2.65	15.3	2.18	76	484	3.63	164	–	Negative	Positive
12	7.44	4.66	2.13	0.04		91	268	0.23	–	–	Positive	–
13	17.57	15.51	1.19	35.71	54.27	64	599	1.01	–	–	Negative	Negative
14	6.61	4.68	0.99	0.38	0.02	91	364	4.67	28	–	Negative	Negative

Lk: leukocytes; Nt: neutrophils; Ly: lymphocytes; CRP: C-reactive protein; Pct: procalcitonin; PI: prothrombin index; IL-6: interleukin 6; PCRc19: SARS-CoV-2 polymerase chain reaction. Altered levels: lymphocytes <1.5 x 1,000/µl; CRP >1 mg/dl; procalcitonina >0.5 ng/ml; PI <75%; fibrinogen >400 mg/dl; D-Dimer >0.5 mg/L; ferritin >140 ng/ml; IL-6 >7 pg/ml.

At physical exploration, seven patients had widespread abdominal pain and five patients had selective pain at the right iliac fossa (RIF). Five patients had signs of peritoneal irritation at abdominal palpation. Some patients also had cutaneous manifestations such as macular rash and petechiae.

Regarding vital signs, the most frequent findings included increased temperature (5/14), tachycardia (10/14), and low blood pressure (10/14). Following the initial assessment by the pediatrics department, a new assessment was requested to the pediatric surgery department in eight patients.

A blood test (Table II) and a PCRc19 test were carried out in all patients, 4 of whom had a positive result. Serological analysis was performed in nine highly suspicious patients, with SARS-CoV-2 immunoglobulin G (IgG) being found in four patients. Therefore, eight patients had confirmed diagnosis of COVID-19, whereas six patients had suspected diagnosis based on compatible clinical criteria.

Further microbiological tests were conducted in all patients, with a single incidental finding – a *Staphylococcus hominis* positive blood culture.

Abdominal ultrasonography was requested given the suspicion of acute appendicitis in five cases, and the suspicion of peritonitis in four cases. In one case, abdominal ultrasonography was performed in order to rule out pyelonephritis, and in other four cases, as a complementary test with no specific clinical suspicion. Ultrasound findings demonstrated unspecific inflammatory signs in virtually all patients (Table III).

An abdominal CT-scan was carried out in four patients, with findings being similar to those noted at ultrasonography – unspecific inflammation of the terminal ileum, the ileocecal valve and the ascending colon, with free fluid at the RIF, and gallbladder wall edema. One of the CT-scans demonstrated appendicular inflammation, which was reported as acute appendicitis.

The assessment was complemented with thoracic X-ray examination in eleven patients. It demonstrated a pattern of peribronchial infiltrate with bilateral involvement in four patients and unilateral involvement in one patient.

Seven patients were admitted at the Pediatric Hospitalization Room (PHR), most of whom had a favorable evolution. Abdominal symptoms progressively improved, and enteral nutrition was resumed following a mean of 27.6 hours. One of the patients admitted at the PHR required PICU admission as a result of hemodynamic instability. In total, eight patients required PICU admission, seven of whom were referred directly from the emergency department as a result of hemodynamic instability, with a rapid worsening. Mean PICU stay was 5 days, and oral feeding was resumed following a mean of 33 hours. Treatment was symptomatic in all cases, with non-invasive oxygen therapy being applied in 7 out of 14, volume expansion in 10 out of 14, vasoactive drugs in 5 out of 14, and mechanical ventilation in 1 out of 14. In eleven patients, given the suspicion of abdominal sepsis, empirical antibiotic treatment was initiated, and in seven patients, COVID-19 targeted treatment (lopinavir/ritonavir, hydroxychloroquine, and azithromycin) was implemented.

Table III. Abdominal ultrasound findings.

Patient	*Appendix*	*Other structures*
1	Not visualized	–
2	Complicated appendicitis	Gallbladder edema
3	Not visualized	Gallbladder edema
4	Not visualized	Inflammation of the terminal ileum and the cecum, and free fluid at the RIF
5	Normal appendix	Gallbladder edema, inflammation of the ileum, the ascending colon and the sigmoid colon, and mesenteric fat
6	Not visualized	Gallbladder edema, inflammation of the terminal ileum and the cecum, and mesenteric fat
7	Not visualized	Gallbladder edema, free fluid at the RIF
8	Normal appendix	Lymphadenitis at the RIF
9	Normal appendix	Lymphadenitis at the RIF
10	Not visualized	Inflammation of the ileum, the ileocecal valve and the ascending colon, and lymphadenitis at the RIF
11	Not visualized	Inflammation of the cecum, and lymphadenitis and free fluid at the RIF
12	Normal appendix	–
13	Not visualized	Lymphadenitis at the RIF
14	Normal appendix	–

One patient required surgery as a result of having ultrasound findings of complicated appendicitis, apart from physical exploration being compatible with acute abdomen. An exploratory laparoscopy was performed. It demonstrated a normal appendix and signs of acute cholecystitis, with an inflammatory plastron in the area. Postoperative evolution was poor, with persistent abdominal pain and oral feeding not being resumed until 8 days later. However, she never had respiratory involvement or hemodynamic instability.

DISCUSSION

Our study consisted of a group of patients with abdominal pain, which was mostly widespread or located at the right iliac fossa, associated with fever, vomit, and diarrhea. These symptoms are a common reason for consultation at pediatric emergency departments, with a wide array of differential diagnoses[1]. Inaccurate diagnosis may lead to complications as a result of unnecessary surgery or treatment delay. In our healthcare facility, the abdominal pain management protocol establishes the patient is initially assessed by the pediatrician, who requests the relevant diagnostic tests; and in the presence of suspected surgical pathology, the patient is referred to the pediatric surgery department. In our series, abdominal ultrasonography was carried out in all patients, and surgeon assessment was requested in half of them – in spite of the absence of acute appendicitis signs. Surgeon assessment was requested because clinical signs, along with general condition and blood test results, led to suspected complicated appendicular pathology. As a result of pediatric care redistribution, the number of patients with surgical acute abdomen managed at the emergency department increased by 35%, with a frequency of 4-6 daily appendicitis cases undergoing surgery in that period. A significant number of acute appendicitis patients had advanced clinical signs, such as widespread abdominal pain and pain at the RIF, with signs of sepsis. Therefore, following patient assessment, the diagnostic and therapeutic process was speeded up, with an urgent ultrasonography request and early empirical antibiotic treatment initiation, as established by the protocol from our healthcare facility. At subsequent physical exploration by the surgeons, widespread abdominal pain and voluntary contraction were noted, but without clear signs of peritoneal irritation. Consequently, a conservative approach was decided upon in all cases, except for the patient diagnosed with complicated acute appendicitis following ultrasonography. All patients undergoing pediatric surgery assessment belonged to the first half of the study period, with a significant decrease in cross-consultations subsequently. Patients undergoing abdominal CT-scan for ultrasound finding confirmation purposes also belonged to the first half of the study period, since patient general condition raised important doubts in terms of diagnosis at that time. Probably, the evolution of the first patients made further imaging tests and initial surgical assessment unnecessary in the second half of the study period. This can be explained by the fact COVID-19 has been included in acute abdomen differential diagnosis in the presence of similar clinical, ultrasound, and blood test findings.

COVID-19 digestive symptoms have been previously described both in adult and pediatric patients[2,3]. The action mechanism causing these symptoms is seemingly related to the binding capacity of SARS-CoV-2 spike protein to angiotensin-converting enzyme 2 (ACE2) receptors when penetrating into the cells. ACE2 receptors regulate inflammation, and they are expressed both in the respiratory airways and in various cell lines, including the intestinal epithelium and the vascular endothelium. Intestinal epithelium and vascular endothelium alteration favors vasoconstriction, causing edema in the organs involved and stimulating hypercoagulability, which may lead to tissue ischemia. Both mechanisms could account for digestive symptoms directly caused by intestinal epithelium inflammation and indirectly caused by vascular involvement[4-6].

Regarding radiological findings, the unspecific inflammation of the terminal ileum, the ileocecal valve, and the ascending colon is worth noting. These findings have been previously described in other COVID-19 patients[7,8]. They are related to direct cell involvement as a result of the aforementioned inflammatory reaction, and to vascular involvement as a result of capillary microthrombosis or partial mesenteric artery occlusion. These studies report intestinal wall involvement, intestinal pneumatosis, and biliary stasis[8]. Gallbladder inflammation was a frequent finding in the first half of the study period, but it was not found in the remaining patients.

Blood test disorders were similar to those reported in other series[9], with increased levels of acute-phase reactants such as CRP and especially procalcitonin. Even though procalcitonin is a bacterial infection marker, increased levels were found in 90% of patients from our sample, despite the absence of bacterial coinfections (except in one patient). This finding has not been reported in adult patients. The remaining blood test results were similar to those described in adults, with low lymphocyte levels and high D-Dimer and ferritin levels.

PCRc19 test results were positive in very few cases. Therefore, analyzing other data, such as clinical record, blood test results, and imaging tests, proves essential for early suspected diagnosis and support treatment initiation. Some authors recommend a thoracic CT-scan is carried out in these patients to complete diagnosis, since radiological findings are highly characteristic and occur at the initial stage[10]. In general, the PCRc19 diagnostic sensitivity reported by countries has been variable and does not exceed 90%. Consequently, highly clinically suspicious patients should be considered positive in spite of having a negative test result[11].

COVID-19 cutaneous manifestations have been described and classified[12,13], which means they can help achieve diagnosis when present.

In terms of patient evolution, it should be highlighted that various patients had complications and required PICU admission and vital support. Patient evolution was compatible with pediatric inflammatory multisystem syndrome (PIMS), which was first described in early April in an American patient and subsequently reported in many EU countries[14-17], with symptoms similar to those found in Kawasaki disease. In the series published, patients frequently had fever, abdominal pain, and other gastrointestinal symptoms, and less often, conjunctivitis, cutaneous rash, and shock. In these patients, respiratory symptoms were rare. Blood test findings described in other countries are analogous to those found in our patients. Similarly, many of the cases reported had a PCRc19 test negative result, and diagnosis was achieved by analyzing clinical records and compatible findings[14]. From the pediatric surgeon's standpoint, the cases in our series were not easy to discriminate from acute abdomen cases caused by early-stage appendicular peritonitis. Therefore, opting for a non-surgical, conservative approach was a difficult decision. In spite of the limitations inherent to observational, retrospective studies, there are two key aspects for an accurate differential diagnosis to be achieved. On the one hand, imaging tests should be carried out in order to identify both the appendix and other intra-abdominal disorders, avoiding diagnoses entirely based on physical exploration[18]. And on the other hand, collecting further epidemiological, clinical, and blood test data potentially leading to COVID-19 diagnosis proves of the upmost importance[19]. In our view, conservative treatment with regular reassessment[20] is the most adequate approach. Therefore, even though CT-scan had demonstrated acute appendicitis in one of our patients, a non-surgical approach was decided upon as clinical signs were not characteristic of appendicular pathology, but mostly compatible with PIMS as a result of COVID-19. In cases like this, even with evidence of acute appendicitis at imaging tests, if the patient is in poor general condition and there is hemodynamic instability, we believe opting for a non-surgical approach with intravenous antibiotic treatment to relieve the appendicular pathology and avoid complications associated with surgery under general anesthesia in such conditions is the right decision.

Regarding the only patient undergoing surgery, it should be noted that even though she did not require hemodynamic support and had no symptoms compatible with PIMS, digestive symptoms (abdominal pain and vomit) disappeared later than in patients without PIMS not undergoing surgery (8 days *vs.* 24 hours). Surgical side-effects such as increased local inflammation, presence of pneumoperitoneum, paralytic ileus, and wound pain most likely contributed to symptom persistence.

CONCLUSIONS

Abdominal pain is a frequent reason for consultation at pediatric emergency departments, with a wide array of differential diagnoses, including surgical pathology. The

new coronavirus infection can bring about digestive symptoms as the first manifestation, simulating acute abdomen. Therefore, being able to identify this is important to initiate early treatment, since it may have a poor evolution and cause PIMS, which may seriously compromise the patient's life. A good clinical record and a comprehensive physical exploration should be performed, blood tests and imaging tests should be analyzed in search of findings characteristic of COVID-19, and other abdominal pathologies should be ruled out. PCRc19 virus detection was little sensitive in our series. Consequently, even if results are negative, if the remaining data are highly suspicious of SARS-CoV-2 infection, the patient should be considered positive in terms of differential diagnosis and decision-making.

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