Acute Appendicitis in Multisystem Inflammatory Syndrome in Children With COVID-19

Key Words: COVID-19, MIS-c, appendicitis

To the Editors:

South Africa has the highest number of COVID-19 cases in Africa to date with Cape Town as the initial epicenter. Up to 20 August 2020, 78 children with positive polymerase chain reaction (PCR) severe acute respiratory syndrome (SARS)-CoV-2 were admitted to Tygerberg Hospital in Cape Town. We present 4 of these children, 5- to 12-years-old age (2 males) with appendicitis and confirmed SARS-CoV-2 on PCR of respiratory specimens (Table 1). Three children were initially diagnosed with acute appendicitis and treated surgically and multisystem inflammatory syndrome in children (MIS-c) was diagnosed in all three after appendectomies. The fourth child was admitted with clinical appendicitis and tested for SARS-CoV-2 due to hospital policy but was managed non-surgically and did not have MIS-c.

Similar to a recent case series from London, we highlight that children with COVID-19 may present with clinical features suggestive of appendicitis or atypical appendicitis as part of MIS-c.[1,2] Cases 1 and 2 were included in a recent report on MIS-c in Cape Town, and all children were diagnosed with appendicitis during a time where an increase in these case was identified in our center.[2] However, unlike children from London, all children with MIS-c and appendicitis were PCR positive for SARS-CoV-2. Moreover, children in the London series were diagnosed with terminal ileitis and none required surgery.[1] In our series of MIS-c, 3 of the children had surgically confirmed appendicitis (Table 1): 2 with complicated appendicitis with perforation and intra-abdominal pus and the third was confirmed histologically.

TABLE 1. Clinical and Laboratory Characteristics of Children With Appendicitis and Positive SARS-CoV-2 on Respiratory Specimen

Case	1	2	3	4
Age	8	5	12	8
Sex	F	F	M	M
SARS-CoV-2 PCR	Positive	Positive	Positive	Positive
Diagnosis	MIS-C Complicated acute appendicitis	MIS-C Complicated acute appendicitis	MIS-C Uncomplicated acute appendicitis	— Uncomplicated acute appendicitis
Signs and symptoms				
Duration of symptoms prior to surgery	1	1	3	N/A
Fever	+	+	+	+
Abdominal pain	+	+	+	+
Vomiting	+	–	–	+
Diarrhea	–	–	–	+
Rash	+	+	+	–
Conjunctival injection	+	+	+	–
Shock	+	+	+	–
Surgery				
Findings at surgery	Perforated appendix with pus in 4 quadrants.	Perforated appendix. Pus in pelvis and lower abdomen.	Hyperemia No pus or signs of abscess formation. Mesenteric lymph node	N/A
Histology	Not available	Acute appendicitis with perforation and peritonitis.	Acute appendicitis with peritonitis. Acute lymphadenitis with microabscess formation.	N/A
Laboratory findings				
CRP (peak)	500 mg/L	238 mg/L	112 mg/L	14 mg/L
Ferritin (peak)	1361 ug/L	611 ug/L	544 ug/L	106 ug/L
D-Dimer (peak)	>17.6 mg/L	17.6 mg/L	5.7 mg/L	—
Pro-BNP (peak)	3158 ng/L	-	282 ng/L	—
Troponin T (peak)	8 ng/L	-	21 ng/L	—
Creatine kinase	1144 U/L	-	1096 U/L	—
Lymphocytes (nadir)	0.37×10^9/L	0.86×10^9/L	0.72×10^9/L	—
Urea (initial)	19.7 mmol/L	4.6 mmol/L	3.3 mmol/L	6.8 mmol/L
Creatinine (initial)	146 umol/L	25 umol/L	54 umol/L	53 umol/L
Albumin (nadir)	23 g/L	22 g/L	31 g/L	—
Blood culture	Neg	Neg	Neg	Neg
Management				
Intensive care	+ (4 d)	+ (1 d)	High care	–
Inotropic support	+	+	+	–
IVIG	+	+	+	–
Steroid pulse	+	+	+	–
Aspirin	+	+	+	–
Antibiotics	+	+	+	+
Respiratory support	Ventilated for 2 days followed by 2 days high flow oxygen.	Nasal prong oxygen	–	–
Duration of hospitalization (d)	10	11	7	4
Imaging				
Echocardiogram findings	Normal left ventricular function (ejection fraction = 70%). Both coronary arteries echobright, within normal size.	Dilated coronary arteries. Ejection fraction 62%.	Mild impairment of left ventricular systolic function (ejection fraction 52%), coronary arteries not dilated.	-

The possible relationship of viral entry through angiotensin-converting enzyme 2 receptors, abundantly present

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in the terminal ileum, and its relationship with terminal ileitis has been well documented.[3] What is not clear, is whether appendicitis may occur as a complication of SARS-CoV-2 through similar proposed mechanisms related to the inflammation associated with viral entry or reactive lymphoid hyperplasia causing luminal obstruction. Acute appendicitis is known to be associated with Kawasaki disease, of which MIS-c shares many common clinical and pathologic features, possibly related to appendicular artery vasculitis.[4] In Kawasaki disease, abdominal features may represent more severe disease.[5] No fecoliths were found in any of the children requiring appendectomy, possibly supporting inflammation or vasculitis as pathologic mechanism.

Where surgical emergencies are not managed in conjunction with pediatricians, surgeons should familiarize themselves with the features of MIS-c to facilitate early identification and referral of possible cases. The importance includes the impact on diagnosis of appendicitis, postoperative recovery, and the management of multisystem involvement, which differentiates this entity from the regular course of isolated acute appendicitis. Our experience suggests that, as with Kawasaki disease, pediatricians that diagnose MIS-c should be vigilant and continue to carefully evaluate children for surgical complications, including appendicitis and perforation, particularly if abdominal pain is part of the presenting complaint. Access to sophisticated imaging to differentiating appendicitis from terminal ileitis may be limited in some settings, but if there is doubt the most sophisticated available imaging should be sought.

Our experience further highlights the suspected association between acute appendicitis, COVID-19, and MIS-c. This should always be considered particularly in children with clinical appendicitis who are PCR positive for SARS-CoV-2 at the time of presentation.

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REFERENCES

1. Tullie L, Ford K, Bisharat M, et al. Gastrointestinal features in children with COVID-19: an observation of varied presentation in eight children. *Lancet Child Adolesc Health*. 2020;4:e19–e20.
2. Webb K, Abraham DR, Faleye A, et al. Multisystem inflammatory syndrome in children in South Africa. *Lancet Child Adolesc Health*. 2020;S2352-4642(20)30272-8. doi: 10.1016/S2352-4642(20)30272-8. Online ahead of print.
3. Ni W, Yang X, Yang D, et al. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. *Crit Care.* 2020;24:422.
4. Garnett GM, Kimball S, Melish ME, et al. Appendicitis as the presenting manifestation of Kawasaki disease. *Pediatr Surg Int.* 2014;30:549–552.
5. Fabi M, Corinaldesi E, Pierantoni L, et al. Gastrointestinal presentation of Kawasaki disease: a red flag for severe disease? *PLoS One*. 2018;13:e0202658.

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To the Editors:

As of August 24, 2020, a total of 23,800,692 cases and 816,534 deaths due to COVID-19 have been reported worldwide,[1] and Latin America has become the new pandemic epicenter. Globally, 5 Latin American countries are among the top 10 in terms of total cases: Brazil, Peru, Mexico, Colombia, and Chile. Of these, Brazil and Mexico are among the 3 leading countries with more deaths globally. Therefore, urgent indexed publications are needed from Latin America, including those related to children.

We read the recent call for data for South America by Antúnez-Montes[2] and investigators from 6 Latin American countries and Italy and agree on the need for regional data. However, we call for the inclusion and expansion of research in more centers from Mexico, Central America, the Caribbean, and other South American countries. In August 2020, the REKAM-LATINA network (Red de Enfermedad de Kawasaki en América Latina) started the REKAMLATINA-3 study, an ambispective multinational study focused on MIS-C in Latin American children and adolescents. Ours is the largest multinational multicenter integrated Kawasaki disease research network, in terms of number of pediatric subspecialties (11), researchers (304), and countries (20): Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Uruguay, and Venezuela.[3,4] To date, investigators from 161 main pediatric and general referral hospitals have confirmed their participation.

MIS-C cases have been reported so far in all Latin American countries of the network (unpublished data, REKAM-LATINA researchers' personal communications). However, few specific MIS-C reports have been published[5] and overwhelming COVID-19-related work, time limitations, and English-language barriers have been and will be major obstacles for multicenter publications from Latin America. To obtain robust data for this study, we have integrated investigators from REKAMLATINA, Sociedad Latinoamericana de Infectología Pediátrica (SLIPE), Asociación Latinoamericana de Pediatría (ALAPE), Sociedad Latinoamericana de Emergencia Pediátrica (SLEPE), Red de Investigación y Desarrollo de la Emergencia Pediátrica Latinoamericana (RIDEPLA), Latin American Pediatric Intensive Care Network (LARed Network), Sociedad Latinoamericana de Cuidados Intenstivos Pediátricos (SLACIP), and other national