Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Multisystem inflammatory syndrome in SARS-CoV-2 infection mimicking acute appendicitis in children

Dear Editor,

A 7 years old boy with no known comorbidities was presented to our attention with complaints of low-grade fever and conjunctivitis for 5 days. In the previous 48 h, he had developed gastroenteritis-like symptoms and hyperpyrexia associated with asthenia and anorexia.

The father, a medical doctor, was asymptomatic, while the mother, a biologist, had been experiencing anosmia for one month. He accessed the Emergency Department in April 19, 2020. His abdomen was tense and painful and micro-petechial eruptions were obvious on his limbs.

The patient's laboratory findings were: white blood cells count was 11500/mm^3; Hemoglobin (Hb) was 11.8 g/dl; platelets (PLTs) were 75000/mm^3; C-reactive protein (CRP) was 347 mg/L; procalcitonin (PCT) was 49 ng/ml; D-dimer was 6031; and fibrinogen was 708 mg/dl. Real Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) test for SARS-CoV-2 infection was negative.

The patient was admitted for observation and further investigations. During the first night as inpatient, he underwent sudden hypoxia (oxygen saturation <85%) and hypotension, with a systolic blood pressure of 80 mmHg.

He was transferred to the Intensive Care Unit where he developed an inflammatory vasculitis associated with a precongestive heart failure, leading to a heart profile enlargement at echocardiography, with pericardial effusion (Fig. 1).

Inotropes were started and endocrinological consultation was done. The specialist (endocrinologist) suggested a multisystem inflammatory syndrome in children (MIS-C). Thus, a steroid treatment was administered (2 mg/kg/day intravenous methylprednisolone for 1 week, followed by 1.5 mg/kg/day oral prednisolone for an additional 1 week).

Due to the atypical features, he underwent two SARS-Cov-2 tests (RT-PCR) (both negative) and one dosage of seric Immunoglobulin G (IgG) for SARS-Cov-2 (positive).

Repeated abdominal ultrasounds revealed a thickening of appendiceal wall without peritoneal free fluid and diffuse thickening of terminal ileum and colon associated with adenomesenteritis (lymphadenopathy and inflammatory fat throughout the mesentery).

During the hospitalization, the general conditions progressively improved without airways intubation and mechanical ventilation.

The cardiac inotropes were gradually stopped and echocardiography was normal, with minimal residual pericardial effusion (4 mm).

1. Discussion

SARS-CoV-2 is the causative agent of Coronavirus Disease 2019 (COVID 19). It binds to Angiotensin-Converting Enzyme type-2 (ACE-2) receptor in order to gain entry into the human cells.[1] In infected patients, the clinical presentation depends on tissue distribution of these receptors. ACE-2 is widely expressed on lung alveolar epithelial cells and small intestinal epithelial cells; therefore, the main symptoms are respiratory and gastrointestinal. Gastrointestinal involvement is very common in children, while respiratory distress is most common in adults.[2]

Over the past months, several cases of new MIS-C correlating with SARS-CoV-2 infection have been documented among pediatric population.

MIS-C definition includes six diagnostic criteria: serious illness leading to hospitalization, age <21 years, fever lasting for at least 24 h, laboratory evidence of inflammation, multisystem organ involvement, evidence of SARS-CoV-2 infection based on RT-PCR, antibody testing, or exposure to persons with Covid-19 in the past month.[3]

This emerging entity shows similar features with those of toxic shock syndrome and atypical Kawasaki disease.[4] It occurs about 4—6 weeks after acute SARS-CoV-2 infection, developing from an uninhibited immune response to a prior infection rather than acute manifestation of the viral disease. Among the initial symptoms, high fever and

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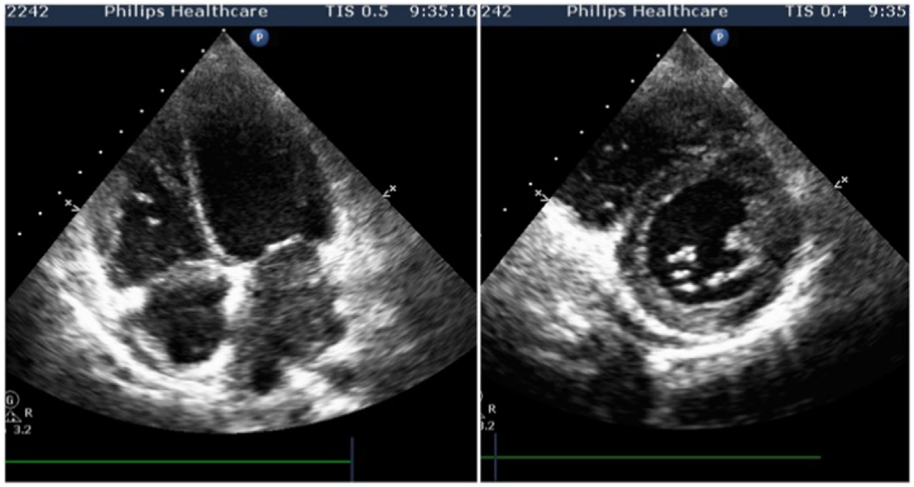

Figure 1 Echocardiography demonstrating heart profile enlargement with mild pericardial effusion.

gastrointestinal impairment (that is, abdominal pain, vomiting, and diarrhea) correlate with high values of CRP (>100 mg/L), requiring differential diagnosis of acute appendicitis. When it is neither recognized nor properly treated, it may lead to a left ventricular dysfunction, coronary aneurisms, and heart failure.[4]

From our experience, gastrointestinal impairment seems to differ from the traditional presentation of appendicitis. Although abdominal pain is not electively localized in the right iliac fossa, it is more diffuse and often presents symptoms like vomits and diarrhea. Moreover, levels of CRP detected in the blood are extremely high (>200 mg/L), this is uncommon in pediatric patients with acute appendicitis. Abdominal ultrasound shows indirect signs of appendicitis like mesenteric lymphadenopathy or borderline thickening of appendicular wall. Since the hyper-inflammatory syndrome develops after the acute viral event and despite the fact that nasopharyngeal and rectal swab turn out to be negative, at least IgG detected in the blood of these patients are quite high.[5]

In conclusion, routine serological test for SARS-CoV-2 should be performed in infants with unusual abdominal pain and elevation of inflammatory markers and who had no diagnosis of appendicitis, since early detection and treatment of SARS-CoV-2 hyper-inflammatory syndrome is vital for prompt management.

Compliance with ethical standards & submission statements

- No grant was received for this study.
- Informed consent was obtained from all individual participants (children's parents) included in the study.

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the Institutional and National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Declaration of competing interest

None. All Authors declare that they have no conflict of interest.

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