Abdominal pain in covid times: time to think twice

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Abstract

We report a case of abdominal pain followed by acute systolic heart failure due to multisystem inflammatory syndrome in children (MIS-C). This multisystem disease typically appears several weeks after infection with COVID-19 in children and young adults. There is a wide spectrum of presentation with MIS-C: some present with features of shock, others with a condition that has overlapping characteristics with Kawasaki disease (KD), and others with more non-specific features. Very often the symptoms include gastrointestinal symptoms. Our 17-year-old patient presented with fever, abdominal pain and inflammatory laboratory results. Rapidly after admission he developed acute heart failure with biopsy-confirmed myocarditis. The diagnostic criteria of MIS-C were met. This case emphasizes the changing diagnostic landscape. However rare, we want to raise awareness for MIS-C in children and young adults presenting with abdominal pain. Because of the risk of rapid clinical deterioration, early recognition and a multidisciplinary approach can be life-saving. (Acta gastroenterol. belg., **2022,** 85, **400-402**).

Keywords: COVID-19, PIMS, MIS-C, myocarditis.

Introduction

Coronavirus disease 2019 (COVID-19) is known to affect all age groups, but the disease morbidity and mortality is generally less severe in children than in adults. However, there is emerging evidence for the appearance of a severe multi-system inflammatory syndrome after SARS-CoV-2 infection (1). The condition was first reported in April 2020 and has been studied and described increasingly ever since. The Royal College of Pediatrics and Child Health (RCPCH) first defined this condition as "Pediatric inflammatory multisystem syndrome – temporally associated with SARS-CoV-2" (PIMS-TS) (2). The World Health Organization (WHO) developed a resembling definition for "multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19" (3). A similar entity was defined by the Centers for Disease Control (CDC) as the "multisystem inflammatory syndrome in children" (MIS-C). MIS-C is currently considered the official name of the disease (4). We present a case of initially isolated abdominal pain, with afterwards development of cardiac involvement and acute heart failure. Besides a COVID-19-related condition, there is no other explanation for the events. The diagnostic criteria for PIMS-TS are met.

Case history

A 17-year-old male patient was admitted to the emergency department due to severe abdominal pain since two days, with vomiting and general deterioration. Besides an oligosymptomatic covid-19 infection four weeks ago, he had no relevant medical history. The pain occurred suddenly and he also reported nausea, non-bloody diarrhea and a sore throat. He denied upper or lower respiratory tract symptoms, urinary symptoms or skin rash. Vital signs at the time of examination included a temperature of 38.1 °C, blood pressure of 126/75 mmHg, heart rate of 78 bpm, respiratory rate of 15/min and oxygen saturation of 97% on room air. Clinical examination revealed a non-tender abdomen, with painful palpation of the right iliac fossa. Laboratory analysis (shown in Table 1) was remarkable for an inflammatory syndrome with elevated CRP (110.0 mg/L) and lymphopenia, high ferritin levels, high procalcitonin and

Table 1.

Laboratory markers	Result	Normal range
Hemoglobin (g/dL)	16.4	13.0-17.0
White cell count (x 10^3/L)	7.71	3.90-9.90
- neutrophils	6.55	- 1.80-8.00
- lymphocytes	0.66	- 1.5-5.20
- monocytes	0.40	- 0.20-0.60
- eosinophils	0.00	- 0.03-0.46
- basophils	0.04	- 0.02-0.09
Thrombocyte (x 10^3/L)	155	162-351
D-dimer (ng/mL)	6822	<500
PT (%)	67	7030-116.0
PT (INR)	1.32	0.85-1.15
aPTT	38	28-39
Fibrinogen (mg/dL)	658	180-400
Bicarbonate (mmol/L)	23.6	22.0-29.0
Ureum (mg/dL)	40	17-48
Creatinine (mg/dL)	1.73	0.67-1.17
CK (U/L)	461	<190
LDH (U/L)	393	135-225
CRP (mg/L)	111.0	0.0-5.0
Ferritin (µg/L)	1085	30-400
Procalcitonin (ng/mL)	6.76	<0.10
Albumin (g/L)	35.5	35.0-52.0

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Submission date: 03/01/2021
Acceptance date: 14/02/2021

mild thrombocytopenia. D-dimer levels were 6822 ng/mL. Furthermore there were an elevated creatinine level (1.73 mg/dL), elevated total CK level and LDH. A CT of the abdomen was first interpreted as acute appendicitis and the patient was scheduled for laparoscopic surgery. Review of the CT however suggested absence of appendicitis, but mesenteric adenitis with signs of abscess formation was suspected. The patient was admitted to the pediatric department with intravenous (IV) fluids and antibiotics (amoxicillin/clavulanic acid 1g every 6 hours). 24 hours after admission the patient continued having a fever (up to 39,1 °C) and he developed hemodynamic instability, unresponsive to IV hydration. The patient was admitted to the intensive care unit (ICU) for intensive monitoring, IV rehydration and antibiotics were empirically switched to ceftriaxone (2g every 24 hours). Inotropic support was not necessary yet. Because ECG now showed signs of anterolateral repolarization abnormalities, in combination with elevated troponin (0,260 ng/dL) and NT-proBNP levels (4925 pg/mL), a transthoracic ultrasound was performed. This confirmed acute heart failure with severely diffuse hypocontractility of the left ventricle with a measured LVEF of 30%. Diastolic LV function was normal and there was no pericardial effusion. Coronarography revealed no coronary stenosis or aneurysm. A myocardial biopsy (Figure 1) was performed and pathology examination was consistent with viral myocarditis, showing an elevated interstitial cellularity with mononuclear cells, some neutrophils and eosinophils. A PCR on the myocardial biopsy could not detect SARS-CoV-2 E/N/RdRP-genes. MRI of the heart confirmed the reduced LVEF (37%) with myocardial edema on T1-/T2-mapping. With supportive treatment there was a rapid clinical, biochemical and haemodynamical improvement. The patient could leave the hospital 7 days after hospital admission. Extensive auto-immune and viral testing was negative, bacterial cultures remained sterile. A COVID-19 PCR was negative, but antibodies tested IgG positive and IgM negative.

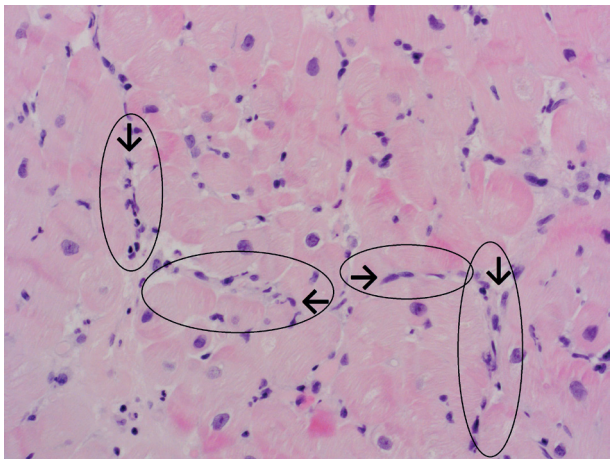

Figure 1. — Endomyocardial biopsy (hematoxylin eosin stain, x 200): an increased number of inflammatory cells (lymphocytes, neutrophils and an occasional eosinophil) are seen in between the myocytes. Ischemic changes or necrosis are not present.

Table 2

Proposed Case Definitions for the Hyperinflammatory Syndrome Associated With Covid-19

RCPC *(2)*

A child presenting with persistent fever, laboratory evidence of inflammation and evidence of single or multi-organ dysfunction. This may include children fulfilling full of partial criteria for Kawasaki disease.

Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus.

SARS-CoV-2 PCR testing may be positive or negative

WHO *(3)*

Children and adolescents 0-19 years of age with fever > 3 days

AND two of the following:

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet)

2. Hypotension or shock

3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponine/NT proBNP)

4. Evidence of coagulopathy (by PT, PTT, elevated D-dimer)

5. Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)

AND elevated markers of inflammation such as ESR, CRP of procalcitonin

AND no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal of streptococcal shock syndromes

AND evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

CDC *(4)*

An individual aged < 21 years presenting with fever, laboratory evidence of inflammation and evidence of clinically severe illness requiring hospitalization, with multisystem(≥ 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
1. Fever ≥ 38.0 °C for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours
2. Laboratory evidence (but not limited to) of one or more of the following: an elevated CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, LDH, or interleukin 6, elevated neutrophils, reduced lymphocytes and low albumin.

AND no alternative plausible diagnoses

AND positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; Or COVID-19 exposure within 4 weeks prior to onset of symptoms

Discussion and conclusion

Initial reports show the benign course of COVID-19 disease in children (5,6). Since April 2020 however there has been an emerging detection of a new multisystem inflammatory illness affecting children, related to COVID-19, with overlapping features of Kawasaki disease, toxic shock syndrome, haemophagocytic lymphohistiocytosis and macrophage activation syndrome. The disease typically appears 4 to 6 weeks after an acute COVID-19-infection. Different definitions exist, defined by the CDC (MIS-C), RCPCH (PIMS-TS) and WHO (multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19). Diagnostic criteria can be found in Table 2. Variations of the definitions are due to the novelty of this condition and the relatively small number of cases described. In addition, the causal association with SARS-CoV-2 infection has not been firmly established, but it is suggested by the temporal association with the current COVID-19 pandemic (1). One of the hypotheses is that MIS-C is a post-infectious process caused by non-neutralizing IgG antibodies through antibody-dependent enhancement (ADE) (7). Reports show that most patients, like the patient in our case, have IgG antibodies to SARS-CoV-2 rather than positive virus detection on nasopharyngeal RT-PCR (1). This post-infection hypothesis also explains why the myocardial PCR in this case tested negative for SARS-CoV-2. A second hypothesis is a delayed excessive cytokine storm in patients with a previously high viral load, caused by the ability of SARS-CoV-2 to block interferon I and III responses (7).

There is a broad spectrum in the presentation of the condition. The main signs and symptoms include persistent fever, gastro-intestinal complaints, muco-cutaneous involvement, as well as severe disease including myocardial injury, shock and coronary artery aneurysms (8). Several case series of patients with MIS-C have been published, showing the large number of patients presenting with abdominal complaints in the early presentation, in particular abdominal pain, nausea and diarrhea. In one study with 58 patients in the UK, 31 (53%) complained of severe abdominal pain and 30 (52%) had diarrhea (1). In Paris, a study describes 20 patients with MIS-C who developed acute myocarditis and severe abdominal pain and required PICU admission. All of them presented fever and severe abdominal pain as first symptoms (9). The same results are noted in a US study with 33 patients, where 32 (97%) of them complained of severe abdominal pain at presentation (10). Other, smaller, case series confirm this observation. Typically the patients have persistent fever (24-72 hours) and have inflammatory lab results. As shown in our case, the differential diagnosis with acute appendicitis is not always easy. This stresses the importance of good visualization of the appendix on ultrasound and/or CT of the abdomen (11). Early recognition of MIS-C is important because the clinical condition can rapidly deteriorate. In our case, there was a rapid spontaneous recovery, but often patients need invasive mechanical ventilation, inotropic support or (rarely) even extracorporeal membrane oxygenation (12). There is currently no evidence on which treatments (e.a. immunomodulatory therapy) could be beneficial, but the multisystem involvement indicates the need for a multidisciplinary approach and early admission in an ICU environment.

In conclusion, abdominal pain in covid times requires the need to think twice. We tried to increase the awareness of this COVID-19 related disease occurring in older children and predominantly presenting with abdominal complaints, fever and possibly with a rapid evolution to hemodynamic instability and myocardial dysfunction. Further research is warranted regarding to pathophysiology, optimal treatment strategies and knowledge on long-term outcome.

Conflict of interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

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