

A Common Problem During the Pandemic Period; Multisystem Inflammatory Syndrome in Children or Gram-negative Sepsis?

To the Editor:

Multisystem inflammatory syndrome in children (MIS-C) is thought to be a delayed, erratic immune response to SARS-CoV-2, rather than a viral-mediated clinical image.¹ MIS-C should be suspected in children presented with a fever and who have at least 2 of the following involvement of cardiac, vascular, respiratory, neurological, hematologic, or dermatologic with high-acute phase reactant.² Because of the nonspecific diagnosis criterion, it should be separated from diseases such as bacterial and viral infections, sepsis, and toxic shock, which are more common in children. With this letter, I wanted to draw attention to the fact that there should be no other alternative disease when diagnosing misc.

CASE 1

A 2-year-old boy was admitted to the hospital with fever, diarrhea, and vomiting. Physical examination showed dry mouth mucosa and reduced turgor tonus. With the diagnosis of acute gastroenteritis, intravenous fluid support was initiated, and his symptoms improved during the follow-up. On the fifth day of his hospitalization, fever and diarrhea returned, along with tachycardia and tachypnea. In controlled laboratory tests, hemoglobin 9.6 g/dL, leukocyte 13,500/mm³ (neutrophil 10,820/mm³, lymphocyte 1350/mm³), thrombocyte 41,000/mm³, C-reactive protein 217 mg/L (0–5), pro-brain natriuretic peptide (BNP) 11,363 pg/mL (0–320), D-dimer 8.9 mg/L (0–0.5), PT 20.3 seconds, aPTT 52 seconds, INR 1.73, ferritin 356 ng/mL, triglyceride 288 mg/dL. Fever, diarrhea, tachycardia, leukocytosis, neutrophilia, lymphopenia, thrombocytopenia, high CRP, high D-dimer, coagulopathy, increased pro-BNP, ferritin, and triglyceride values when the studied SARS-CoV-2 IgG positive. For the patients who matched the

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Table 1. MIS-C Criteria at the Time of Diagnosis

	Case 1	Case 2
Age	2 yrs	5 yrs
Fever	38.5°C	39°C
Multisystem involvement	Cardiac: pro-BNP↑↑, tachycardia	Cardiac: hypotension, tachycardia pro-BNP↑↑
Inflammatory markers	Gastrointestinal: vomiting Hematologic: d-dimer↑↑ CRP↑↑, fibrinogen↑↑, d-dimer↑↑ ferritin↑↑, LDH↑↑, neutrophilia, lymphopenia	Gastrointestinal: vomiting, AST-ALT↑↑ Hematologic: d-dimer↑↑ CRP↑↑, fibrinogen↑↑, d-dimer↑↑ ferritin↑↑, triglyceride↑↑ LDH↑↑, neutrophilia, lymphopenia
Evidence of SARS-CoV-2 infection	SARS-CoV-2 IgG (+)	SARS-CoV-2 IgG (+)
Absence of alternative diagnosis	(–) <i>Klebsiella oxytoca</i> in blood culture	(–) <i>Pseudomonas aeruginosa</i> in urine culture

MIS-C criteria, intravenous immunoglobulin and methylprednisolone therapy were started. Meropenem therapy was started due to the possibility of healthcare-associated bacteremia. In the follow-up, clinical and experimental results soon returned to normal. In blood culture taken during the fever, growth of *Klebsiella oxytoca* was confirmed. Meropenem and methylprednisolone treatments were completed after 14 days and discharged successfully.

CASE 2

A 5-year-old boy with a fever and vomiting was described. Upon physical examination, the patient's general health was weak, hypotensive, tachycardic, and circulatory disturbed, as shown by the prolonged capillary refill time. In laboratory tests: Hemoglobin 10.3 g/dL, leukocyte 23,500/mm³ (neutrophil 22,100/mm³, lymphocyte 830/mm³), thrombocytes 169,000/mm³, C-reactive protein: 46 mg/L (0–5), BUN: 39 mg/dL, creatinine: 0.9 mg/dL, AST: 85 μ/L, ALT: 110 μ/L, pro-BNP 35,000 pg/mL (0–320), D-dimer 11.3 mg/L (0–0.5), PT 12 seconds, aPTT 29 seconds, INR 1.23, ferritin 243 ng/mL, triglyceride 516. The patient with a history of COVID-19 contact tested positive for SARS-CoV-2 IgG. The MIS-C conditions were fulfilled by a patient who tested positive for SARS-CoV-2 IgG and had a fever, high-acute phase reactants, and more than 2 organ involvements (hypotension, tachycardia, circulatory disorder, high pro-BNP, and D-dimer). Echocardiography was found to be normal. IVIG, methylprednisolone low-weight heparin, inotrope support, and cefotaxime treatment were initiated in the intensive care unit. The patient in better overall condition was taken to service. *Pseudomonas aeruginosa* growth was detected in urine and blood cultures and started meropenem treatment. His treatment was completed 2 weeks, and he was discharged successfully.

Our cases highlight the diagnostic difficulties that children with febrile disease faced during the COVID-19 pandemic.

Fever, neurologic, skin, and gastrointestinal symptoms are some of the most common symptoms of MIS-C. However, these signs are nonspecific, and they can be caused by acute bacterial and viral infections. A distinctive feature of MIS-C is that multiple organ systems are affected. The most common organs involved are the heart, lungs, gastrointestinal tract, hematology, nervous system, and skin.³ History of COVID-19 contact or PCR, antibody, and antigen positivity is necessary for MIS-C diagnosis (Table 1). The elevated prevalence of SARS-CoV-2 infection in the population complicates the use of the SARS-CoV-2 antibody assay even further. If the SARS-CoV-2 epidemic signs of progress and antibody prevalence rates rise, a positive antibody test does not guarantee an MIS-C diagnosis.⁴ The most important diagnostic criterion that should be emphasized is the absence of another disease such as sepsis, bacterial, viral infections, toxic shock syndrome, and Kawasaki. As a result of the nonspecific case description, several children tend to have MIS-C at first.⁴

In conclusion, since MIS-C involving multiple organs will result in severe disease and death if not detected early, extreme caution should be taken when making a diagnosis. Because of the nonspecific diagnosis criterion, it should be separated from diseases such as bacterial and viral infections, sepsis, and toxic shock, which are more common in children.

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Long Coronavirus Disease in Pediatric Rheumatology

To the Editors:

We read with interest the article by Ashkenazi-Hoffnung et al¹ reporting 90 children with long coronavirus disease (COVID) followed in a designated multidisciplinary clinic. The authors reported mainly respiratory symptoms with less than half of tested patients carrying abnormal findings.¹ Nevertheless, musculoskeletal manifestations were frequent among the study cohort with myalgia and arthralgia recorded in 46% and 14% of cases, respectively.¹

Herein, we report our experience with long COVID in a tertiary referral hospital for

pediatric rheumatology. We prospectively followed patients referred to our center for musculoskeletal manifestations and a previous severe acute respiratory syndrome coronavirus 2 infection (positive reverse transcription polymerase chain reaction test on nasopharyngeal swab and/or serology tests) from January to June 2021. Six patients (2 girls) were included in the study; the median age at first evaluation was of 10.1 ± 3 years. All patients were previously healthy. None of them was hospitalized because of acute COVID19. All patients underwent a full physical examination along with laboratory test and other investigations according to their clinical manifestations. Polyarthralgia represented the main reason of referral; even so, the clinical pictures were slightly different for each patient. A 10-year-old girl developed diffuse and persistent joint pain along with antalgic gait; all the investigations were negative, and the physical examination documented the presence of allodynia; thus, a diagnosis of diffuse amplified musculoskeletal pain syndrome was made. A 16-year-old boy had persistent low-grade fever with weight loss (7 kg in 3 months) and polyarthralgia of the hands. Three patients had intense joint pain, and one of them, a 5-year-old girl, had an ultrasound documenting an intraarticular swelling of the right hip but the arthralgia persisted once the swelling subsided. One patient was referred for persistent swelling of the fourth toe of the right foot along with a red-purple rash; he was diagnosed as having COVID toe.² The onset of these symptoms preceded or appeared right after a positive result of the nasopharyngeal swab, except for a patient who developed an intense and excruciating low back pain after recovering from a multisystem inflammatory syndrome in children. The median time interval from onset of manifestations and first visit at our center was 2.5 ± 1 months. All patients recovered during the follow-up, and the median duration of long COVID manifestations was 5 ± 1.3 months.

None of our patients developed a chronic inflammatory condition, and the investigations did not document relevant and/or persistent abnormalities. Despite the fact that they all recovered, these patients showed several degrees of limitations in daily life for some months. Furthermore, we recently saw a high number of young patients referred for musculoskeletal manifestations without any abnormal findings, often diagnosed with amplified musculoskeletal pain syndrome, without any antecedent COVID history. Whether long COVID can be considered just a consequence of a viral infection or should be attributed to the implications of “the pandemic era” we are now living in is still a matter of debate.^{3,4}

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Invasive *Haemophilus influenzae* Type b in an Infant During the COVID-19 Pandemic: The Return of Diseases We Hoped Never to See Again...

To the Editors:

A 7-month-old previously healthy female was admitted to our hospital with generalized tonic-clonic seizures, 4 days history of fever (102.9 F) and nonbilious nonbloody emesis. Meningitis was diagnosed with a lumbar puncture that revealed pleocytosis. Brain magnetic resonance imaging with

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