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Characteristics of The Children with a Preliminary Diagnosis of MIS-C: What is The Final Diagnosis?

MIS-C Ön Tanısı Konulan Çocukların Özellikleri: Kesin Tanı Nedir?

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Abstract

Objective: Multisystem inflammatory syndrome in children (MIS-C) is a newly defined acute febrile disease with non-specific symptoms and signs of multiple organ involvement and can mimic several diseases. During the pandemic, the increased alertness of clinicians resulted in overdiagnosis and overtreatment of MIS-C. In this study, we aimed to evaluate the characteristics of the patients with a preliminary diagnosis of MIS-C based on the current definitions and their final diagnosis.

Material and Methods: A single-center retrospective study was conducted for all hospitalized patients who were initially considered to have MIS-C between December 1, 2020, and December 31, 2022.

Results: The study group consisted of 48 hospitalized patients initially diagnosed as MIS-C according to current guidelines. The patients' median age was 36 months (minimum 6 months, maximum 17 years), and 66.7% (n= 32) were male. All patients had fever on admission, and the median duration of fever before admission was 4 days (minimum 1, maximum 14 days). The second most common symptom was diarrhea (43.8%), followed by vomiting (37.5%), abdominal pain (25%) and cough (18.8%). When the final diagnosis of the patients was evaluated, 42 (87.4%) of them had an infectious disease, and other rare diseases were as follows: rheumatologic disease in 1 (2.1%) patient, acute myeloid leukemia in 1 (2.1%) patient, perforated appendicitis in 1 (2.1%) patient, myocarditis in 1 (2.1%) patient, urticaria in 1 (2.1%) patient, abdominal

Öz

Giriş: Çocuklarda multisistem enflamatuvar sendromu (MIS-C), çoklu organ tutulumunun spesifik olmayan semptomları ve belirtileri olan ve çeşitli hastalıkları taklit edebilen yeni tanımlanmış akut ateşli bir hastalıktır. Pandemi sırasında, klinisyenlerin artan farkındalığı, MIS-C tanısının gereğinde fazla konulmasına ve gereğinde fazla tedavisine yol açtı. Çalışmamızda mevcut tanı kriterleri ile MIS-C ön tanısı olan hastaların özelliklerini ve sonrasında konulan kesin tanıları değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Tek merkezli çalışmamızda 1 Aralık 2020-31 Aralık 2022 tarihleri arasında MIS-C ön tanısı ile hastaneye yatırılan tüm hastalar retrospektif olarak değerlendirildi.

Bulgular: Çalışma grubu, mevcut kılavuzlara göre başlangıçta MIS-C tanısı konulan ve hastaneye yatırılmış 48 hastadan oluşuyordu. Hastaların ortanca yaşı 36 ay (minimum 6 ay, maksimum 17 yıl) idi ve %66.7 (n= 32)'si erkekti. Tüm hastaların yatışta ateşi vardı ve yatıştan önceki ateşin ortanca süresi 4 gündü (minimum 1, maksimum 14 gün). İkinci en sık görülen semptom ishal (%43.8), sonrasında kusma (%37.5), karın ağrısı (%25) ve öksürük (%18,8) idi. Hastaların son tanısı değerlendirildiğinde 42 (%87.4) hastada bir enfeksiyon hastalığı vardı ve diğer nadir hastalıklar ise: 1 (%2.1) hastada romatolojik hastalık, 1 (%2.1) hastada akut miyeloid lösemi, 1 (%2.1) hastada perfore apandisit, 1 (%2.1) hastada miyokardit, 1 (%2.1) hastada ürtiker, 1 (%2.1) hastada abdominal kistik

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cystic lymphangioma in 1 (2.1%) patient. Intravenous immunoglobulin was administered for only 1 (2.1.%) patient due to myocarditis.

Conclusion: Our results emphasize that MIS-C has a heterogeneous clinical spectrum and clinicians should be careful for more probable differential diagnoses of MIS-C to prevent overdiagnosis.

Keywords: Children, COVID-19, multisystem inflammatory syndrome in children, MIS-C, preliminary diagnosis

lenfanjiyom idi. Sadece 1 (%2.1) hastaya miyokardit nedeniyle intravenöz immünoglobulin uygulandı.

Sonuç: Bulgularımız MIS-C'nin heterojen bir klinik spektruma sahip olduğunu ve klinisyenlerin gereğinden fazla tanı koymasını önlemek için MIS-C'nin daha olası ayırıcı tanıları konusunda dikkatli olmaları gerektiğini vurgulamaktadır.

Anahtar Kelimeler: Çocuklar, COVID-19, çocuklarda multisistem enflamatuvar sendrom, MIS-C, ön tanı

Introduction

The pandemic of the coronavirus disease 2019 (COVID-19) led to more than 6.950.000 deaths worldwide (1). Unlike adults, children with COVID-19 generally present as asymptomatic or with mild symptoms (2). After a few months of the COVID-19 pandemic, a new and severe syndrome associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported in some countries and was named multisystem inflammatory syndrome in children (MIS-C). This post-infectious inflammatory syndrome includes the clinical criteria of fever, involvement of two or more organ systems, laboratory evidence of inflammation, and laboratory or epidemiologic evidence of SARS-CoV-2 infection (3,4).

MIS-C can present with shock, cardiac involvement, or severe disease manifestations and can cause mortality in children (5). The pediatric intensive care unit (PICU) admission rate was reported to be between 39.7% and 79.1%, and the mortality rate was between 1.9% and 11.7% in previous reports for children diagnosed with MIS-C (5-9). Early and appropriate treatment is very important in preventing morbidity and mortality of MIS-C (6). It is not easy for clinicians to diagnose MIS-C because it can affect nearly any organ system, and many diseases are included in the differential diagnosis (10).

MIS-C is a new and serious disease, and the COVID-19 pandemic caused increased alertness to MIS-C. Therefore, many laboratory and imaging tests can be performed by clinicians for differential diagnosis. The heterogeneous clinical spectrum of MIS-C can lead to misdiagnosis of MIS-C and overtreatment. Thus, in this study, we aimed to evaluate the characteristics of the patients with a preliminary diagnosis of MIS-C based on the current definitions, their final diagnosis, and the laboratory and imaging tests performed for diagnosis.

Materials and Methods

Study Design and Study Population

A single-center retrospective study was conducted between December 1, 2020, and December 31, 2022, at a tertiary level hospital. It is a referral center for pediatric patients in the Aegean region of Türkiye. MIS-C was diagnosed according to the Turkish Ministry of Health COVID-19 Guideline and Centers for Disease Control and Prevention (CDC) Guidelines (11,12). According to these guidelines, inclusion criteria were as follows: children under 18 years of age with a fever for at least 24 h ≥38.0°C, evidence of clinically severe illness requiring hospitalization, two or more organ systems affected (e.g., cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, and neurological), one or more of the laboratory evidence of inflammation, and laboratory or epidemiologic association to COVID-19. The patients' preliminary diagnosis of MIS-C was made by the pediatric infectious disease specialist according to consultations from the pediatric emergency department or outpatient clinics.

All hospitalized patients who were initially considered to have MIS-C according to current guidelines were evaluated between 1 month and 18 years old. The patients were retrospectively identified through medical records.

Data Collection

A standardized form was used to collect epidemiological data (age, sex, underlying medical conditions), symptoms on admission, laboratory and imaging tests performed for diagnosis, final diagnosis in patients misdiagnosed as MIS-C, prognosis (length of hospital stay, oxygen support, PICU admission, mortality) and treatment. The detection of respiratory viruses was performed by multiplex real-time polymerase chain reaction (PCR) assay (Bosphore Respiratory Pathogens Panel Kit V4, Anatolia Geneworks, Türkiye) of a nasopharyngeal specimen that is capable of identifying pathogens including influenza viruses (influenza A H3N2, influenza A H1N1, and influenza B), parainfluenza viruses (PIVs; PIV-1, PIV-2, PIV-3, and PIV-4), human coronaviruses (CoV OC43, CoV NL63, CoV HKU1, and CoV 229E), respiratory syncytial virus A/B, rhinovirus, human metapneumovirus, enterovirus, bocavirus, adenovirus, *Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumonia, Haemophilus influenzae, Bordetella pertussis, Bordetella parapertusis* and *Moraxella catarrhalis*.

Statistical Analysis

Descriptive statistical analysis was performed using SPSS statistical software (version 25; SPSS, Chicago, IL, USA). Data were expressed as mean ± standard deviation (SD) or median (interquartile range) for continuous variables or percentages for categorical variables. Categorical variables were expressed as number (n) and percentage (%).

This study was approved by the Local Ethics Committee (ethical decision no: 854, date: 11.05.2023).

Results

Demographic Features of the Patients

The study group consisted of 48 hospitalized patients initially diagnosed as MIS-C according to current guidelines. The patients' median age was 36 months (minimum 6 months, maximum 17 years), and 66.7% (n= 32) were male. Four (8.3%) patients had an underlying disease, and the most common underlying disease was nephrological disease (n= 2, 4.2%), followed by congenital heart disease (n= 1, 2.1%) and rheumatologic disease (n= 1, 2.1%). All patients had fever on admission, and the median duration of fever before admission was four days (minimum 1, maximum 14 days). The second most common symptom was diarrhea (n= 21, 43.8%), followed by vomiting (n= 18, 37.5%), abdominal pain (n= 12, 25%), cough (n= 9, 18.8%), rash (n= 5, 10.4%), headache (n= 2, 4.2%), respiratory distress (n= 2, 4.2%), and conjunctivitis (n= 1, 2.1%). Thirty-seven (77.1%) patients had a history of SARS-CoV-2 infection, and 11 (22.9%) patients had epidemiologic evidence of SARS-CoV-2 infection. Table 1 shows the demographic and clinical characteristics of the patients.

Laboratory and Imaging Tests Performed for Diagnosis

When routine laboratory tests were evaluated, complete blood count, biochemistry tests, C-reactive protein test, and coagulation tests were performed for all patients. Procalcitonin test was performed for 32 (66.6%) patients and sedimentation for 45 (89.6%) patients. When serological tests were evaluated, COVID-19 serology test was performed for 40 (83.3%) patients and Epstein-Barr virus/cytomegalovirus serology test for 16 (33.3%) patients. Troponin I and creatine kinase-myocardial band tests were performed in 46 (95.8%) patients.

For differential diagnosis of bacterial infections, blood culture was performed in 40 (83.3%) patients, urine culture in 22 (45.8%) patients, stool culture in 17 (35.8%) patients, and throat culture in 5 (10.4%) patients. When moleculer tests were evaluated, COVID-19 PCR was performed in 22 (45.8%) patients and respiratory multiplex PCR test in 13 (27.1%) patients.

Chest X-ray test was performed for 47 (97.9%) patients, abdominal ultrasonography (USG) for 38 (79.2%), thorax USG for 2 (4.2%), abdominal computed tomography (CT) for 3 (6.3%), thorax CT for 2 (4.2%) and echocardiography (ECHO) for 38

Table 1. Demographic and clinical characteristics of the patients

	All patients (n= 48)
Age, months, median, (range)	36 (6 months-17 years)
Sex, male, n, (%)	32 (66.7)
Underlying diseases, n, (%)	4 (8.3)
Nephrological disease	2 (4.2)
Hypertension	1 (2.1)
Vesicoureteral reflux	1 (2.1)
Congenital heart disease	1 (2.1)
Pulmonary stenosis	1 (2.1)
Rheumatologic disease	1 (2.1)
Familial Mediterranean fever	1 (2.1)
Symptoms, n, (%)	
Fever	48 (100)
Diarrhea	21 (43.8)
Vomiting	18 (37.5)
Abdominal pain	12 (25)
Cough	9 (18.8)
Rash	5 (10.4)
Headache	2 (4.2)
Respiratory distress	2 (4.2)
Conjunctivitis	1 (2.1)
Duration of fever before admission, median, (range)	4 (1-14)
History of SARS-CoV-2 infection, n, (%)	37 (77.1)
Epidemiologic evidence of SARS-CoV-2 infection, n, (%)	11 (22.9)

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

(79.2%). Six patients (12.5%) had multiple ECHOs during hospitalization.

When other tests were evaluated, rotavirus/adenovirus antigen test was performed for 19 (39.6%) patients and urinalysis for 41 (85.4%) patients. Table 2 shows the laboratory

Table 2. Laboratory and imaging tests

Tests	All patients (n= 48)
Routine laboratory tests, n (%)	
Complete blood count	48 (100)
Biochemistry tests	48 (100)
CRP	48 (100)
Procalcitonin	32 (66.6)
Sedimentation	45 (89.6)
Coagulation tests, n (%)	
PT, aPTT, INR	48 (100)
Fibrinogen	48 (100)
D-dimer	48 (100)
Serological tests, n (%)	
COVID-19 serology	40 (83.3)
EBV/CMV serology	16 (33.3)
Cardiac markers, n (%)	
Troponin I	46 (95.8)
CK-MB	46 (95.8)
NT-pro-BNP	5 (10.4)
Cultures, n (%)	
Blood culture	40 (83.3)
Urine culture	22 (45.8)
Throat culture	5 (10.4)
Stool culture	17 (35.8)
Molecular tests, n (%)	
COVID-19 PCR	22 (45.8)
Respiratory multiplex PCR	13 (27.1)
Imagining, n (%)	
Chest X-ray	47 (97.9)
Abdominal ultrasonography	38 (79.2)
Thorax ultrasonography	2 (4.2)
Thorax CT	2 (4.2)
Abdominal CT	3 (6.3)
ECHO	38 (79.2)
Number of patients with multiple ECHOs during hospitalization	6 (12.5)
Others, n (%)	
Rotavirus/adenovirus antigen test	19 (39.6)
Urinalysis	41 (85.4)

CRP: C-reactive protein, aPTT: Activated partial thromboplastin time, PT: Prothrombin time, INR: International normalized ratio, CK-MB: Creatine kinase-myocardial band, NT-pro-BNP: N-terminal-pro-brain natriuretic peptide, PCR: Polymerase chain reaction, EBV: Epstein-Barr virus, CMV: Cytomegalovirus, CT: Computed tomography, ECHO: Echocardiography.

and imaging tests performed for the diagnosis of the study group.

Differential Diagnosis in Patients with a Preliminary Diagnosis of MIS-C, Treatment, and Outcomes

When the final diagnosis of patients with a preliminary diagnosis of MIS-C was evaluated, 42 (87.4%) of them had an infectious disease, and other rare diseases were as follows: Rheumatologic disease in 1 (2.1%) patient, acute myeloid leukemia in 1 (2.1%) patient, perforated appendicitis in 1 (2.1%) patient, myocarditis in 1 (2.1%) patient, urticaria in 1 (2.1%) patient, and abdominal cystic lymphangioma in 1 (2.1%) patient. The patient who was diagnosed with abdominal cystic lymphangioma was a 10-year-old female who presented with a two-day fever, abdominal pain, vomiting, elevated acute phase reactants, and COVID-19 serology positivity. In the follow-up, radiological imaging showed abdominal cystic lymphangioma. The most common infectious disease was upper respiratory tract infection in 18 (37.5%) patients, followed by acute gastroenteritis in 15 (31.3%) patients, bacteremia in 5 (10.4%) patients, bronchopneumonia in 2 (4.2%) patients, and urinary tract infection in 2 (4.2%) patients. In upper respiratory tract infections, *M. catarrhalis* (4.2%) was the most common etiological agent, and in acute gastroenteritis adenovirus (4.2%) was the most common etiological agent. The patient who had a fever for 14 days before admission was diagnosed with adenovirus tonsillopharyngitis.

Intravenous (IV) rehydration was used in 45 (93.8%) of the patients, and IV antibiotics were administered in 30 (62.5%) patients with a median duration of 5 (minimum 2, maximum 17) days. Twenty-two (45.8%) patients received oral antibiotics after discharge. Intravenous immunoglobulin (IVIG) was administered for only 1 (2.1.%) patient due to diagnosis of myocarditis. None of the patients received glucocorticoids. Out of 48 patients, none of the patients required oxygen support or died, but 1 (2.1%) patient was admitted to the PICU. The patient who required PICU was a seven-year-old male who presented with a four-day fever, abdominal pain, vomiting, elevated acute phase reactants, and COVID-19 serology positivity. In the follow-up, defense and rebound were positive in abdominal examination and radiological imaging showed perforated appendicitis, the child had a surgical operation and was transferred to the intensive care unit. The total median length of hospital stay was 4 (1-16) days. Table 3 shows the differential diagnosis in patients with a preliminary diagnosis

Table 3. Differential diagnosis in patients with a preliminary diagnosis of MIS-C, treatment, and outcomes

	All patients (n= 48)
Diagnoses, n, (%)	
Infectious	42 (87.4)
Upper respiratory tract infections	18 (37.5)
Acute otitis media	2 (4.2)
Tonsillopharyngitis	5 (10.5)
Bocavirus	1 (2.1)
Adenovirus	1 (2.1)
Parainfluenza virus	1 (2.1)
Enterovirus	1 (2.1)
Cryptic tonsillitis (AGBHS positive)	1 (2.1)
Rhinosinusitis	3 (6.3)
Moraxella catarrhalis	2 (4.2)
Streptococcus pneumonia	1 (2.1)
Nasopharyngitis	8 (16.6)
Respiratory syncytial virus	1 (2.1)
Unknown microorganisms	7 (14.5)
Acute gastroenteritis	15 (31.3)
Adenovirus	2 (4.2)
Entamoeba histolytica	2 (4.2)
Salmonella enterica	1 (2.1)
Unknown microorganisms	10 (20.8)
Bacteremia	5 (10.4)
Bronchopneumonia	2 (4.2)
Urinary tract infection	2 (4.2)

Table 3. Differential diagnosis in patients with a preliminary diagnosis of MIS-C, treatment, and outcomes (continue)

	All patients (n= 48)
Enterobacter cloacae (ESBL negative)	1 (2.1)
Pseudomonas aeruginosa	1 (2.1)
Others	6 (12.6)
Rheumatologic disease	1 (2.1)
Acute myeloid leukemia	1 (2.1)
Perforated appendicitis	1 (2.1)
Myocarditis	1 (2.1)
Urticaria	1 (2.1)
Abdominal cystic lymphangioma	1 (2.1)
Prognosis	
The total length of hospital stay, days, median, (range)	4 (1-16)
PICU admission, n, (%)	1 (2.1)
Oxygen support, n, (%)	0 (0)
Mortality, n, (%)	0 (0)
Treatment, n, (%)	46 (95.8)
IV rehydration	45 (93.8)
IV antibiotics	30 (62.5)
Ceftriaxone	23 (47.9)
Ertapenem	7 (14.6)
Glycopeptide	2 (4.2)
Metronidazole	2 (4.2)
Clindamycin	1 (2.1)
Duration of IV antibiotics, days, median (min-max)	5 (2-17)
Oral antibiotics after discharge	22 (45.8)
IVIG	1 (2.1)
Glucocorticoids	0 (0)

PICU: Pediatric intensive care unit, ESBL: Extended-spectrum beta-lactamase, ABGHS: Group A beta-hemolytic streptococcus, IV: Intravenous, IVIG: Intravenous immunoglobulin.

of MIS-C, treatment, and outcomes of the patients.

Discussion

In this study, we evaluated 48 pediatric patients who were initially diagnosed as MIS-C but had a final diagnosis other than MIS-C. Infectious diseases (87.4%) were the most common diagnosis in patients with a preliminary diagnosis of MIS-C. The most common infectious disease was upper respiratory tract infection (37.5%) and acute gastroenteritis (31.3%) followed by bacteremia (10.4%). Due to the reason that MIS-C could mimic several diseases and diagnostic challenges, numerous routine laboratory tests, serological tests, molecular tests, cultures, and imaging tests were performed for differential diagnoses in our study group. Our results show that MIS-C has a heterogeneous clinical spectrum and clinicians should be careful for more probable differential diagnoses of MIS-C to prevent overdiagnosis.

MIS-C, a newly identified disease in children that emerged after COVID-19, is a severe and mortal disease. It can rapidly cause multi-organ dysfunction and shock that requires immediate treatment to prevent mortality (4). The main aim of the treatment is to decrease systemic inflammation to prevent mortality and morbidity such as coronary artery aneurysms (3). IVIG, corticosteroids, anticoagulants, and in rare cases, immunomodulators such as anakinra or tocilizumab are recommended for the treatment of MIS-C. The need for rapid diagnosis causes a challenge for clinicians due to its poor prognosis if not treated quickly (3,4).

The COVID-19 pandemic caused an increased alertness to MIS-C for clinicians. It can affect all organ systems and can mimic a lot of diseases. However, the heterogeneous clinical spectrum of MIS-C could lead to overdiagnosis and overtreatment (13). In addition, MIS-C can mask serious diseases which

can be fatal if treatment is delayed such as malignancies or sepsis (10). Steen et al. have reported 11 cases suspected of MIS-C based on the current definitions and finally, three of them were diagnosed with a different disease (13). After MIS-C treatment had already been initiated, their patients were diagnosed with perforated appendicitis, inflammatory bowel disease, and *Pseudomonas aeruginosa* sepsis. They emphasized that current diagnostic criteria lack specificity which leads to misdiagnosis and overtreatment of MIS-C. Similar to their report, one (2.1%) of our patient's final diagnosis was perforated appendicitis and bacteremia was detected in 5 (10.4%) patients. AbdelMassih et al. have presented a case misdiagnosed as MIS-C and mistakenly managed due to the COVID-19 pandemic (14). The final diagnosis of this patient was a large coronary fistula complicated by infective endocarditis and multiple septic pulmonary emboli and they reported the diagnostic bias during pandemia led to initial mismanagement.

Avcu et al. have evaluated 38 patients initially misdiagnosed with MIS-C (10). In their study, the most common final diagnosis was that 71% of the patients had infectious diseases, 15.7% had autoimmune/autoinflammatory disease, and 5.2% had hematologic malignancy. They reported that acute gastroenteritis was the most common infectious cause. Roberts et al have reported 68 children initially evaluated for MIS-C but ultimately not diagnosed with MIS-C (15). In their study group, the most common final diagnosis was bacterial infections in 23 patients, autoimmune/autoinflammatory disorders in 12 patients, and acute viral infections in 10 patients. Similar to these reports, the most common final diagnosis was infectious diseases (87.4%) and the most common infectious diseases were upper respiratory tract infections (37.5%) and acute gastroenteritis (31.3%) in our study. However, in our study, autoimmune/autoinflammatory disease (2.1%) rate and hematologic malignancy (2.1%) rate were lower than reported.

MIS-C mimics several other etiologies than infectious diseases such as malignancy, Kawasaki disease, acute appendicitis, rheumatological diseases, and etc. (16). It has been reported that it can also mimic rare infectious diseases such as abdominal tuberculosis, typhoid fever, and Crimean-Congo hemorrhagic fever (16-18). These challenges for diagnosis cause to need to perform more extensive laboratory testing for final diagnosis and it also leads to unnecessary expensive tests for simple infectious diseases such as upper respiratory tract infections. In our study, for all patients who were misdiagnosed as MIS-C despite routine hematological and biochemistry tests, ECHO was performed in 79.2% of the patients and 12.5% of the patients had multiple ECHOs during hospitalization. When we retrospectively evaluated our cases, we noticed that due to the overdiagnosis of MIS-C, we may have used tests such as ECHO more than necessary. In a case series report, it has been emphasized that these overdiagnoses of MIS-C resulted in overtreatment with expensive IVIG for patients (13). In our study, only one patient received IVIG due to a final diagnosis of myocarditis.

This study had limitations, including its retrospective nature and lack of the advantages of randomized control studies. It was a single-center study, and limited numbers of patients were analyzed. However, our results still show the outcome of COVID-19 pandemic caused increased alertness to MIS-C for clinicians and diagnostic challenges.

In conclusion, MIS-C mimicked severe diseases such as acute myeloid leukemia and perforated appendicitis in our study group. We suggest that if patients diagnosed with MIS-C during the pandemic period underwent many tests for diagnosis and were treated with expensive drugs such as IVIG were retrospectively screened, many of them could be diagnosed with a different disease. MIS-C is difficult to diagnose with current nonspecific definitions, and differential diagnosis is limited by the laboratory test capacity of the health care center. Due to the heterogeneous clinical spectrum of MIS-C, clinicians should be careful for more probable differential diagnoses of MIS-C and overdiagnosis.

Ethics Committe Approval: This study was approved by the Clinical Research Ethics Committee of S.B.Ü İzmir Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital (Decision no: 854, Date: 11.05.2023).

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