ÇOCUKLARDA MULTİSİSTEM İNFLAMATUVAR SENDROM (MIS-C)

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Çocuk Enfeksiyon Hastalıkları Bilim Dalı

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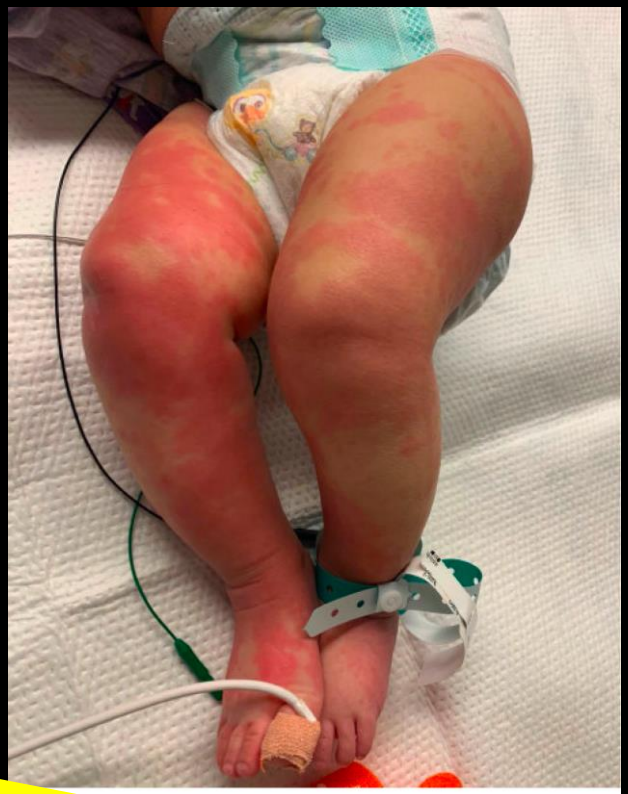
COVID-19 and Kawasaki Disease: Novel Virus and Novel Case

DOI: 10.1542/hpeds.2020-0123

Journal: *Hospital Pediatrics*



rash. Image shared with parental permission.

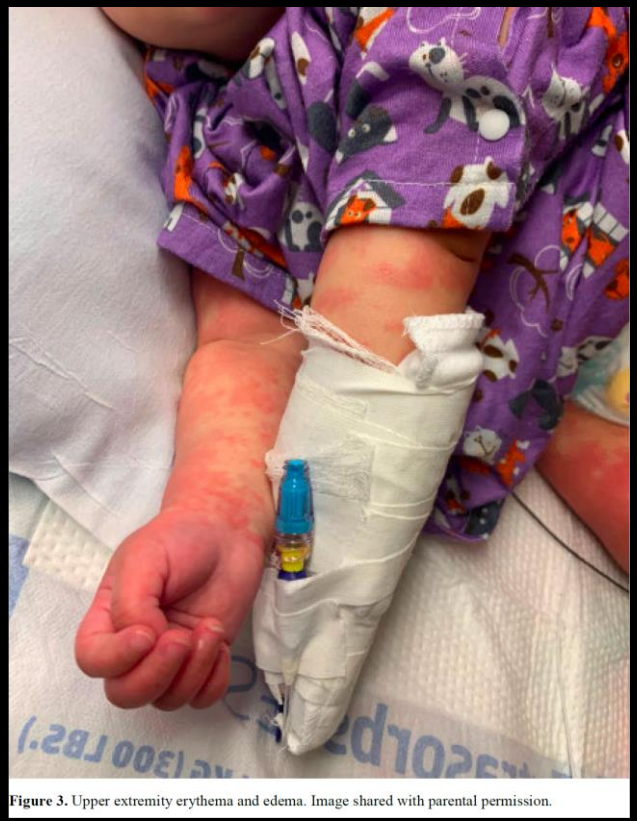


Figure 3. Upper extremity erythema and edema. Image shared with parental permission.

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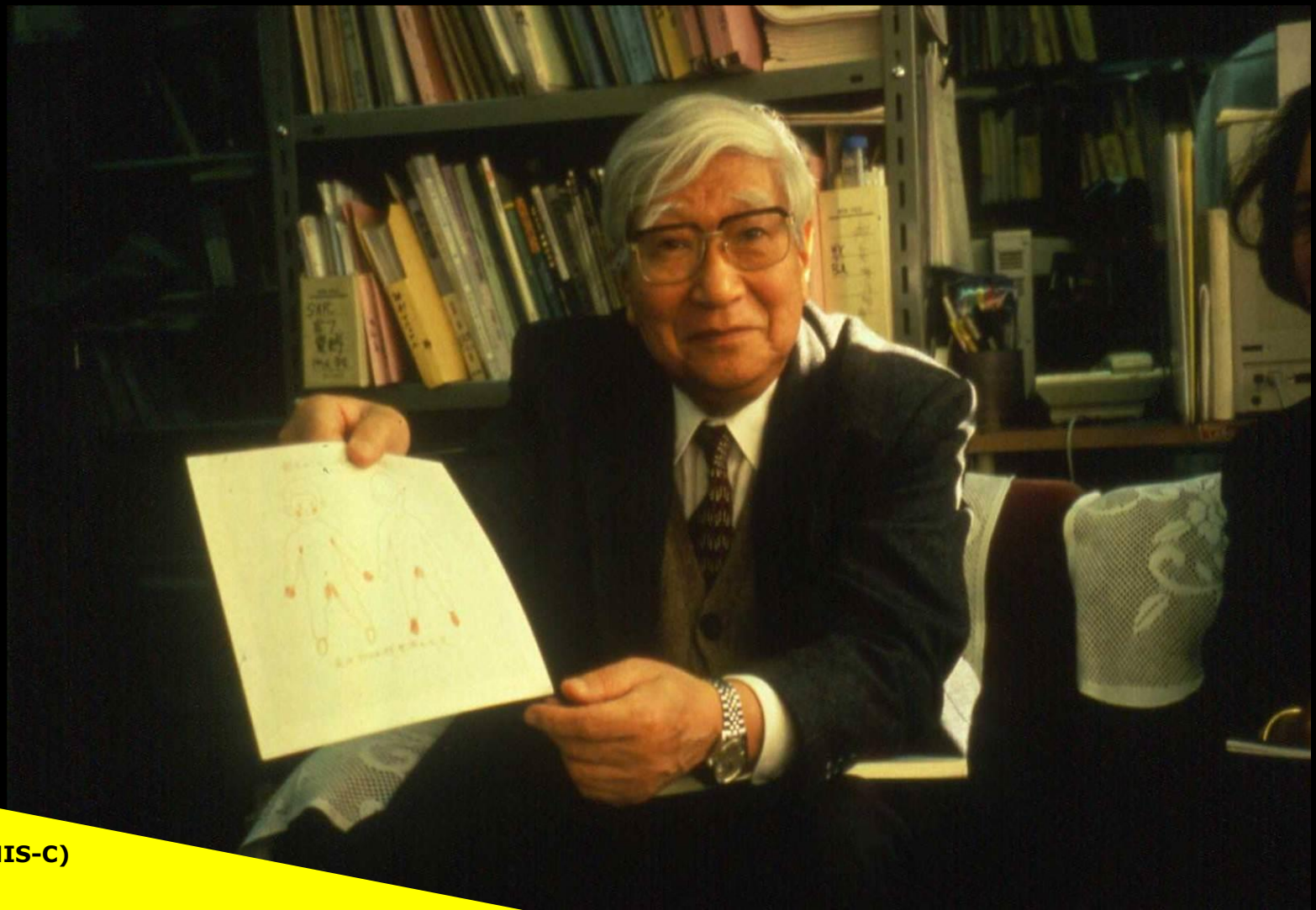

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Kısa Tarihçe

Pediatr Infect Dis J, 2002;21:993–5

Commentary: Translation of Dr. Tomisaku Kawasaki's original report of fifty patients in 1967

JANE C. BURNS, MD

The description in Japanese by Tomisaku Kawasaki of 50 infants and children suffering from a curious new ailment in Japan in the 1960s has now been translated into English and is available for readers at http://www.pidj.com. It is truly a masterpiece of descriptive clinical writing from the past century.[1] In his exhaustive detailing of every observable aspect of the disease, Kawasaki was part Sherlock Holmes and part Charles Dickens with his sense of mystery and his vivid descriptions of the clinical features of these patients. So careful are the daily observations of his patients that when one reads in the detailed description of the first case that the patient "smiled for the first time" on the 26th day of his illness, one is convinced that this is an accurate statement.

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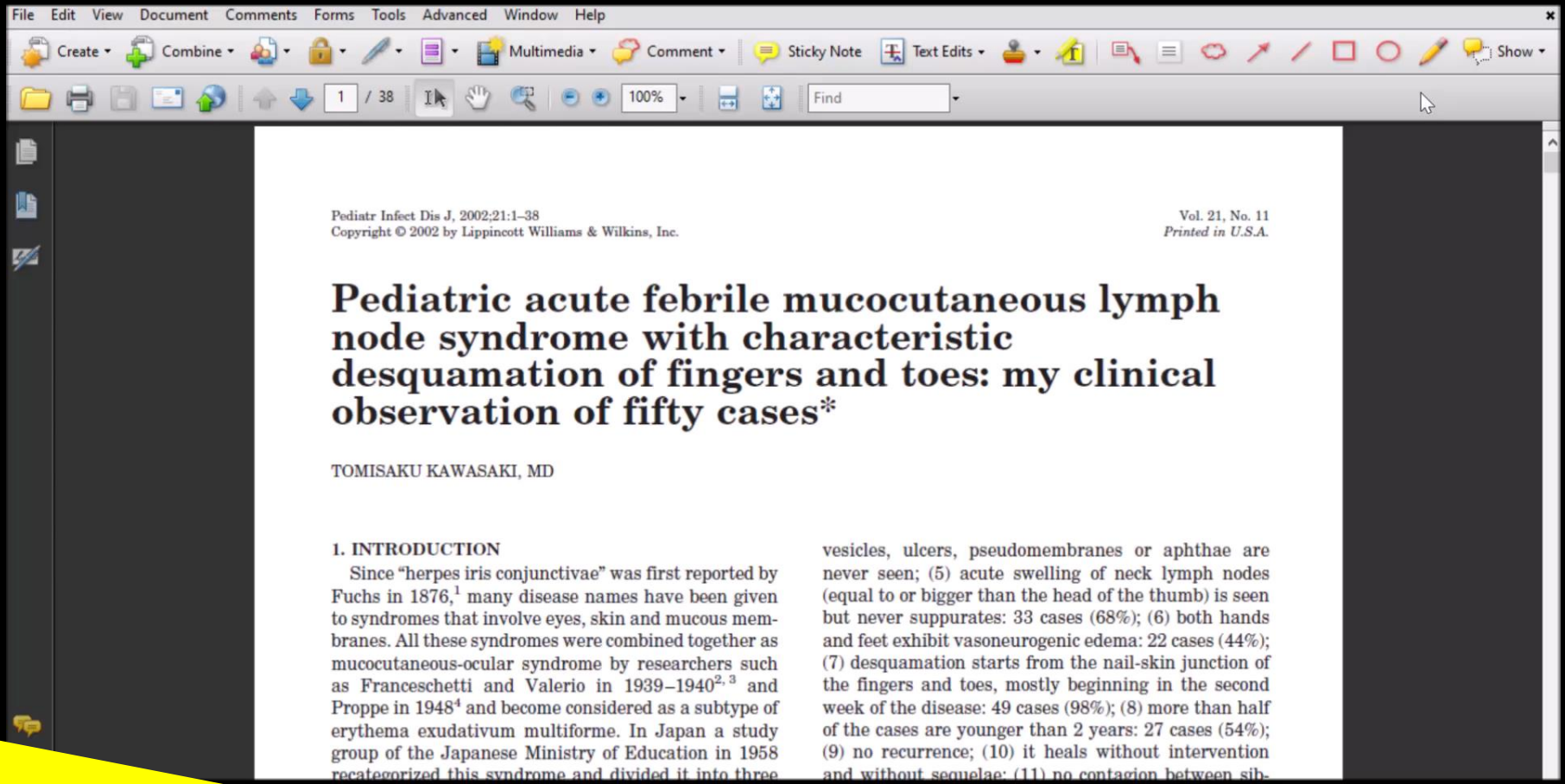

Pediatr Infect Dis J, 2002;21:1–38
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Vol. 21, No. 11
Printed in U.S.A.

Pediatric acute febrile mucocutaneous lymph node syndrome with characteristic desquamation of fingers and toes: my clinical observation of fifty cases*

TOMISAKU KAWASAKI, MD

1. INTRODUCTION

Since "herpes iris conjunctivae" was first reported by Fuchs in 1876,[1] many disease names have been given to syndromes that involve eyes, skin and mucous membranes. All these syndromes were combined together as mucocutaneous-ocular syndrome by researchers such as Franceschetti and Valerio in 1939–1940[2, 3] and Proppe in 1948[4] and become considered as a subtype of erythema exudativum multiforme. In Japan a study group of the Japanese Ministry of Education in 1958 recategorized this syndrome and divided it into three

vesicles, ulcers, pseudomembranes or aphthae are never seen; (5) acute swelling of neck lymph nodes (equal to or bigger than the head of the thumb) is seen but never suppurates: 33 cases (68%); (6) both hands and feet exhibit vasoneurogenic edema: 22 cases (44%); (7) desquamation starts from the nail-skin junction of the fingers and toes, mostly beginning in the second week of the disease: 49 cases (98%); (8) more than half of the cases are younger than 2 years: 27 cases (54%); (9) no recurrence; (10) it heals without intervention and without sequelae; (11) no contagion between sib-

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Classic KD is diagnosed in the presence of fever for at least 5 d (the day of fever onset is taken to be the first day of fever) together with at least 4 of the 5 following principal clinical features. In the presence of ≥4 principal clinical features, particularly when redness and swelling of the hands and feet are present, the diagnosis of KD can be made with 4 d of fever, although experienced clinicians who have treated many patients with KD may establish the diagnosis with 3 d of fever in rare cases (Figure 2):

1. Erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa
2. Bilateral bulbar conjunctival injection without exudate
3. Rash: maculopapular, diffuse erythroderma, or erythema multiforme-like
4. Erythema and edema of the hands and feet in acute phase and/or periungual desquamation in subacute phase
5. Cervical lymphadenopathy (≥1.5 cm diameter), usually unilateral

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ATEŞ

Klasik Kawasaki tanısı en az 5 gün ateşe dayanır.
Tipik bulgular varsa 4 veya 3 gün süren ateş ile tanı konulabilir.
Ateş remittan tiptedir (>39-40°C)
Uygun tedavi verilmezse 1-3 hafta boyunca sürer.
Kendiliğinden 7 günde düşen ateş tanıyı dışlamaz.
Ateş genellikle IVIG infüzyonunu takiben 36 saat içinde düşer.

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Klinik Bulgular

Incomplete Kawasaki disease in an infant presenting with only prolonged fever

Halil Özdemir[1], Aylin Çiftçi[2], Adem Karbuz[1], Ergin Çiftçi[1], Ercan Tutar[3], Semra Atalay[3], Erdal İnce[1]

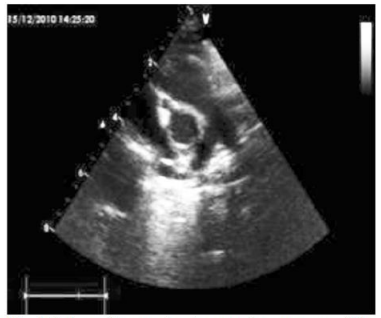

Fig. 1. Echocardiogram showing saccular aneurysm of the right coronary artery (3.5 mm in width).

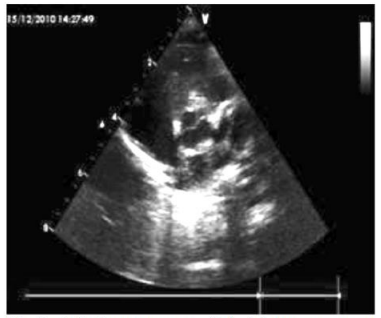

Fig. 2. A fusiform aneurysm of the left coronary artery (4.5 mm in width and 8 mm in length).

A 2.5-month-old boy admitted to our hospital with irritability, poor feeding and fever of 12 hours' duration. On physical examination, he was febrile and extremely irritable. Initial whole blood count revealed a hemoglobin level of 10.1 g/dl, white blood count of 17,800/mm^3 and platelet count of 454,000/mm^3. Erythrocyte sedimentation rate was 80 mm/h and C-reactive protein was 3.96 mg/dl. Biochemical examinations of serum, urinalysis, chest X-ray, and analysis of cerebrospinal fluid (CSF) were normal. He was started on intravenous ampicillin and ceftriaxone empirically for provisional occult bacteremia. His blood, urine and CSF cultures were negative. On the 7th day of the treatment, there were no additional symptoms or findings other than fever. Echocardiography revealed aneurysms in both the left and right coronary arteries. Intravenous immunoglobulin (IVIG) and per oral aspirin were administered, and the fever resolved after IVIG infusion. Two years later, the echocardiography showed disappearing of the saccular aneurysm on the right coronary artery, but the dilatation of the left coronary artery was persisting. In conclusion, incomplete Kawasaki disease should always be included in the differential diagnosis of an infant with persistent fever, especially one younger than three months of age, when the conventional [illegible] fails to reveal the underlying cause.

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Klinik Bulgular

KAWASAKI DISEASE WITHOUT FEVER

Claas H. Hinze, MD, Thomas B. Graham, MD,* and Jamie S. Sutherell, MD†*

Abstract: Kawasaki disease (KD) characteristically presents with prolonged, remittent fever in addition to other clinical findings. We report the case of a 3-month-old boy who developed characteristic manifestations of KD and coronary aneurysms in the absence of fever. This case report underlines the difficulty to diagnose KD in young infants.

Kawasaki Disease Without Fever: A Mild Disease?

Gámez-González Luisa Berenise[1], Rivera-Rodriguez Leonardo[2], García-Pavón Susana[3], Rivas-Larrauri Francisco[4], Yamazaki-Nakashimada Marco[2-4]

Results: Although rare, KD can occasionally present without fever. A total of eleven cases of non-fever KD have been described. The majority of cases do not present major complications. Conclusion:

Classic KD is diagnosed in the presence of fever for at least 5 d (the day of fever onset is taken to be the first day of fever) together with at least 4 of the 5 following principal clinical features. In the presence of ≥4 principal clinical features, particularly when redness and swelling of the hands and feet are present, the diagnosis of KD can be made with 4 d of fever, although experienced clinicians who have treated many patients with KD may establish the diagnosis with 3 d of fever in rare cases (Figure 2):

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DÖKÜNTÜ

Döküntü genellikle ilk 5 gün içinde ortaya çıkar.

- **En sık yaygın makülopapüler döküntü görülür**
- **Scarlatiniform eritroderma**
- **Eritema multiforme**
- **Nadiren ürtikeryal veya mikropüstüler döküntü görülebilir**
- **Büllöz, veziküler ve peteşial döküntü beklenmez**

Döküntü, öncelikle gövde ve ekstremitelerdedir.

Kasık bölgesinde daha belirgin olup daha erken soyulur.

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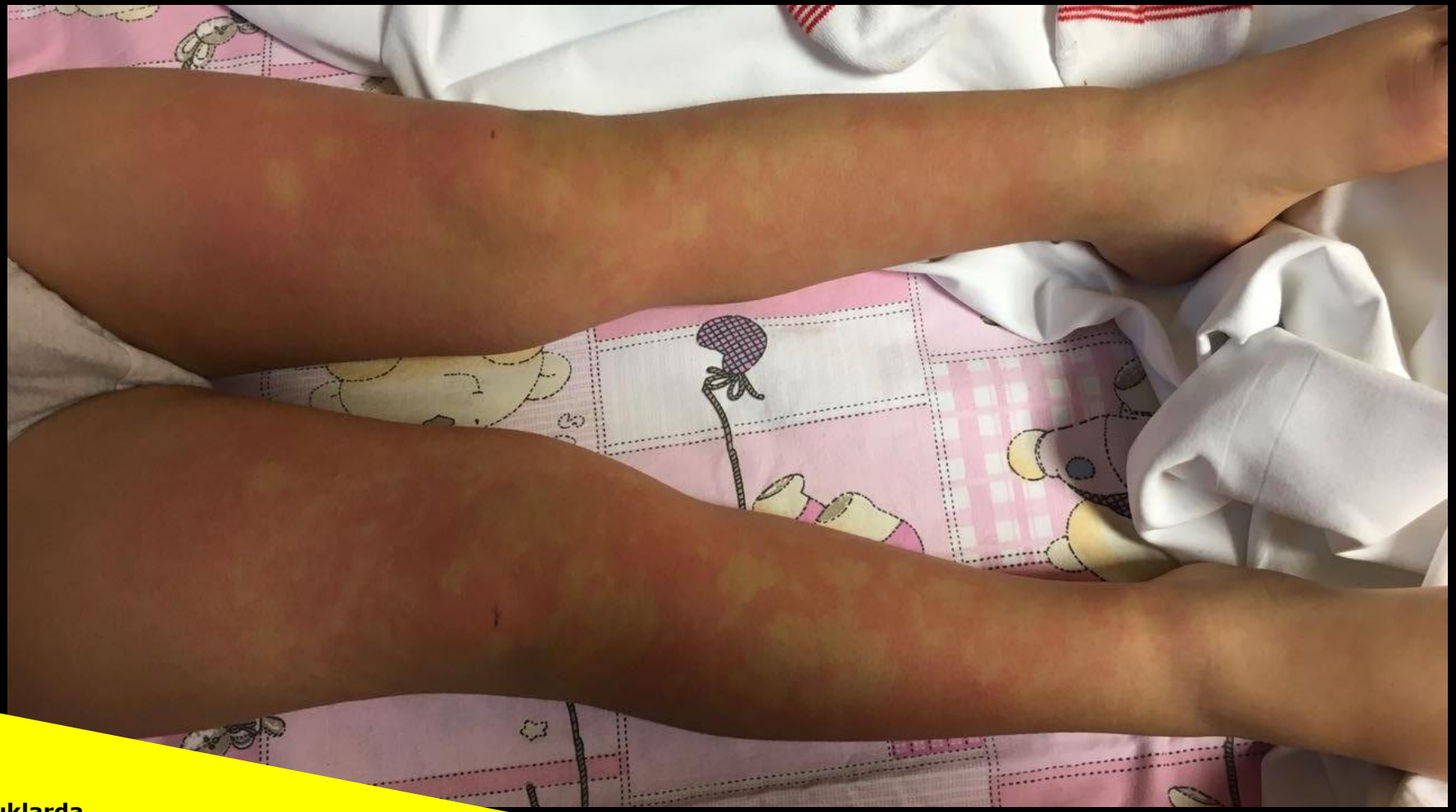

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EKSTREMİTE DEĞİŞİKLİKLERİ

Ekstremitelerdeki değişiklikler en belirgin bulgulardandır.

Avuç içi ve ayak tabanları kızarık, el ve ayakta bazen ağrılı olan endurasyon görülür.

Ateş başlangıcından sonra 2-3 hafta içinde el ve ayak parmaklarından başlayan soyulma görülür.

Ateş başlangıcından 1-2 ay sonra, tırnaklarda derin transvers oluklar (Beau çizgileri) görülebilir.

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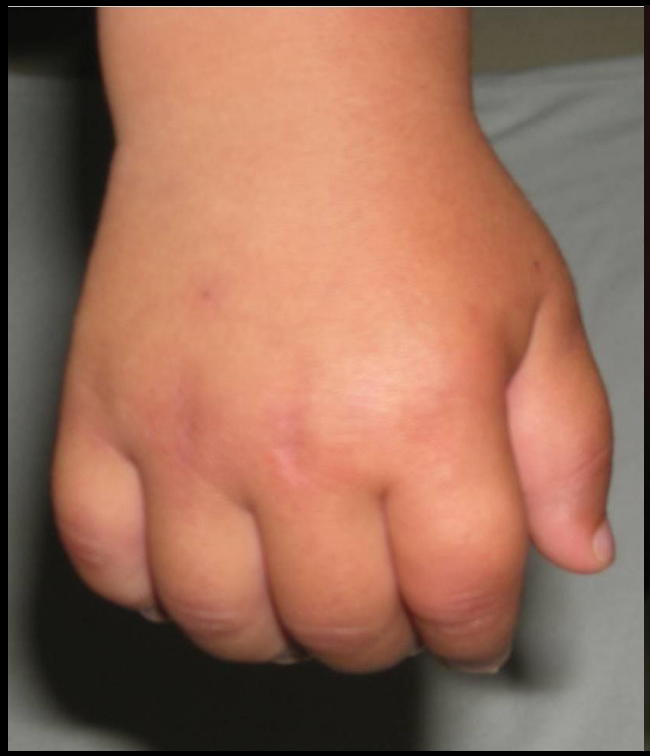

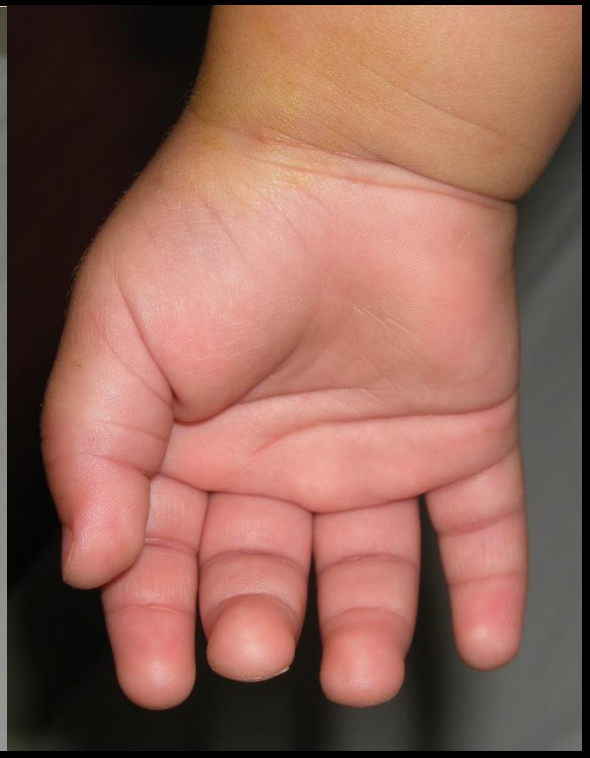

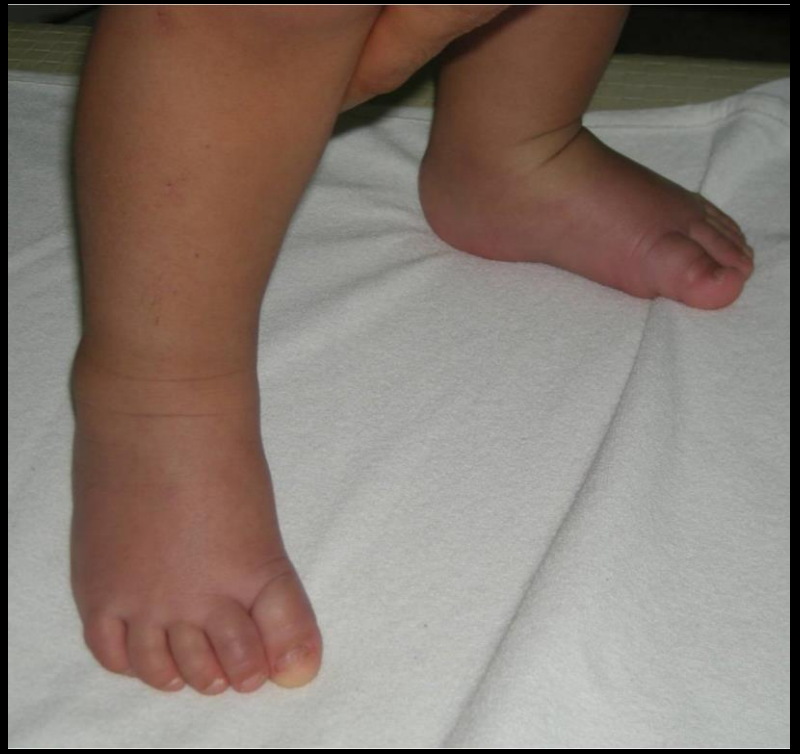

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KONJONKTİVAL KIZARIKLIK
Ateş başladıktan kısa bir süre sonra başlar.
Bilateral bulbar eksudatif olmayan konjonktival kızarıklık görülür.
Sıklıkla iris çevresindeki avasküler limbus bölgesini tutmaz.
Ön üveit (yarık lamba muayenesinde) ateşin ilk haftasında sıktır.
Subkonjonktival kanama ve punktat keratit bazen görülür.

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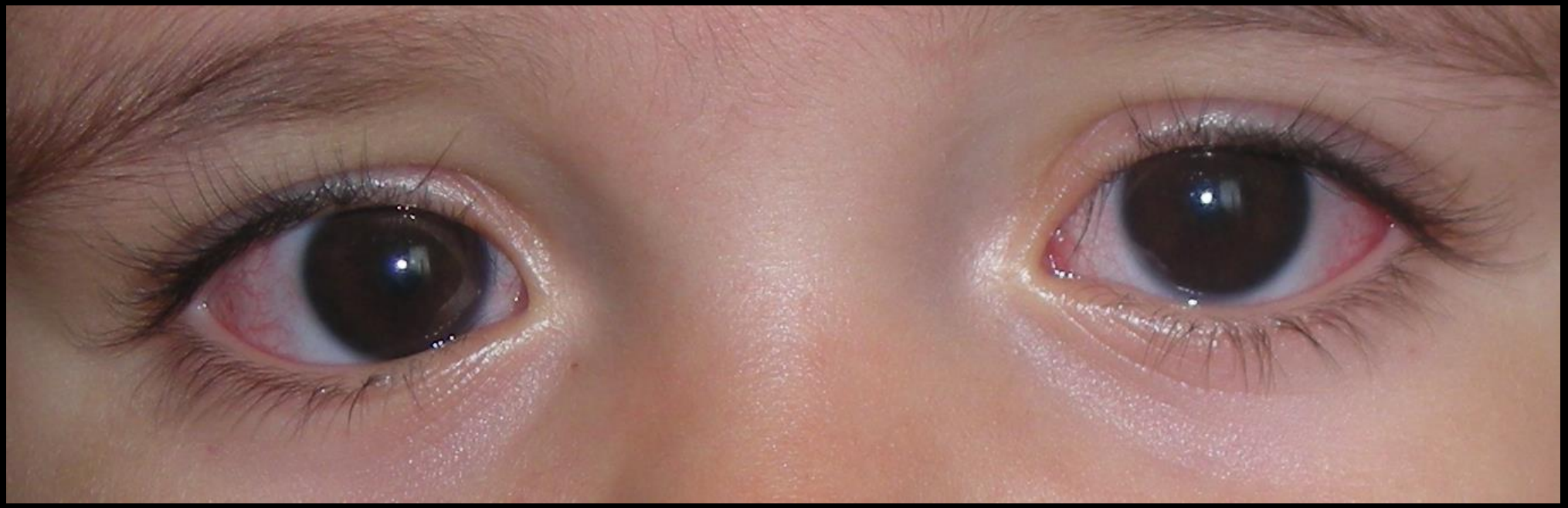

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AĞIZ DEĞİŞİKLİKLERİ

(1) Dudaklarda eritem, kuruluk, çatlama, soyulma ve kanama
(2) Çilek dili: dilde kızarıklık ve fungiform papillar belirgin
(3) Orofaringeal mukozada yaygın kızarıklık

Oral ülserler ve faringeal eksüdalar beklenmez.

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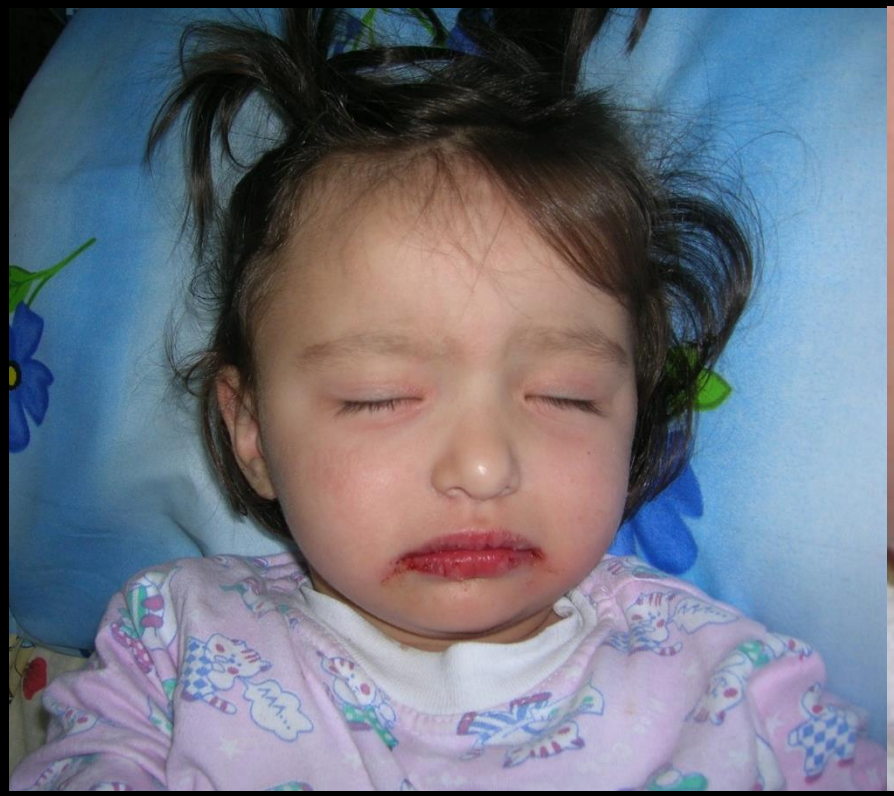

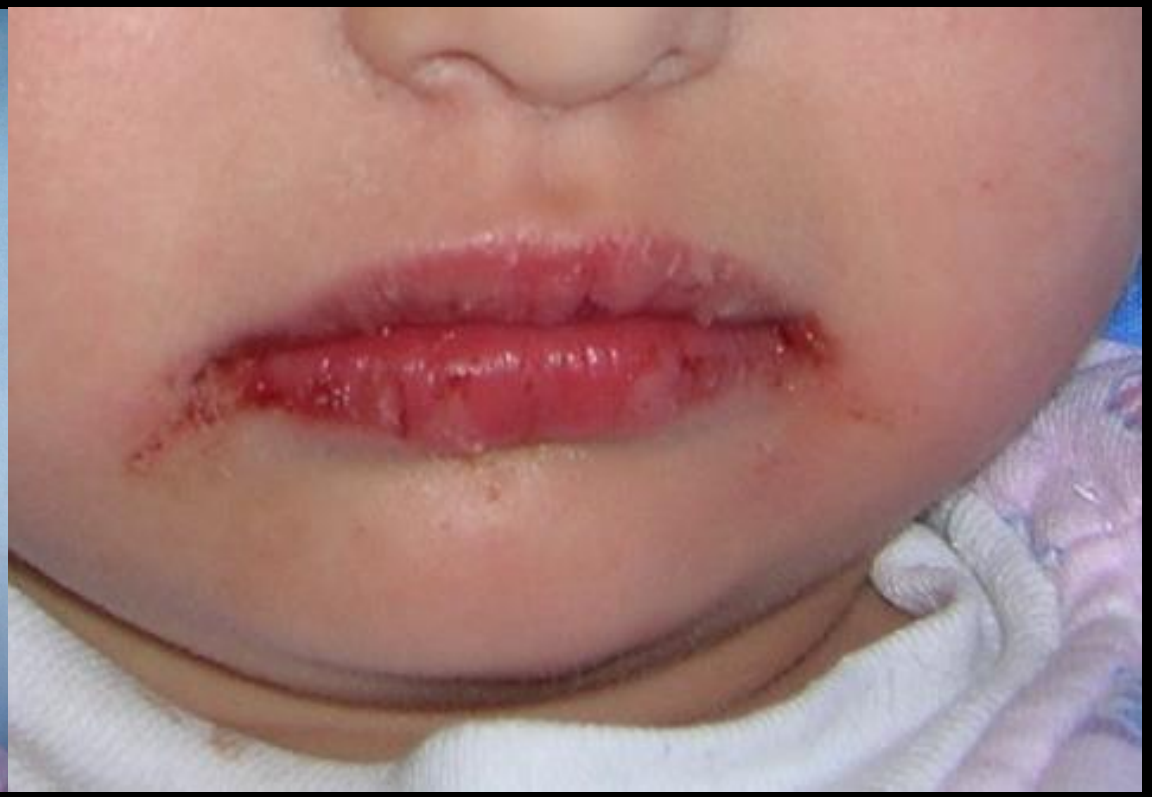

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SERVİKAL LENFADENOPATİ

Servikal lenfadenopati en az görülen tanı kriteridir.

Genellikle tek taraflı ≥1.5 cm çapında, ön servikal üçgen ile sınırlı.

Bazen lenf bezi bulguları en belirgin bulgu olabilir.

- **Bakteriyel lenfadenit düşündürür**
- **Antibiyotiğe rağmen ateş devam eder**
- **Döküntü ve konjonktival kızarıklık gibi diğer bulgular izler**
- **USG ve BT tanıda yardımcı olabilir**

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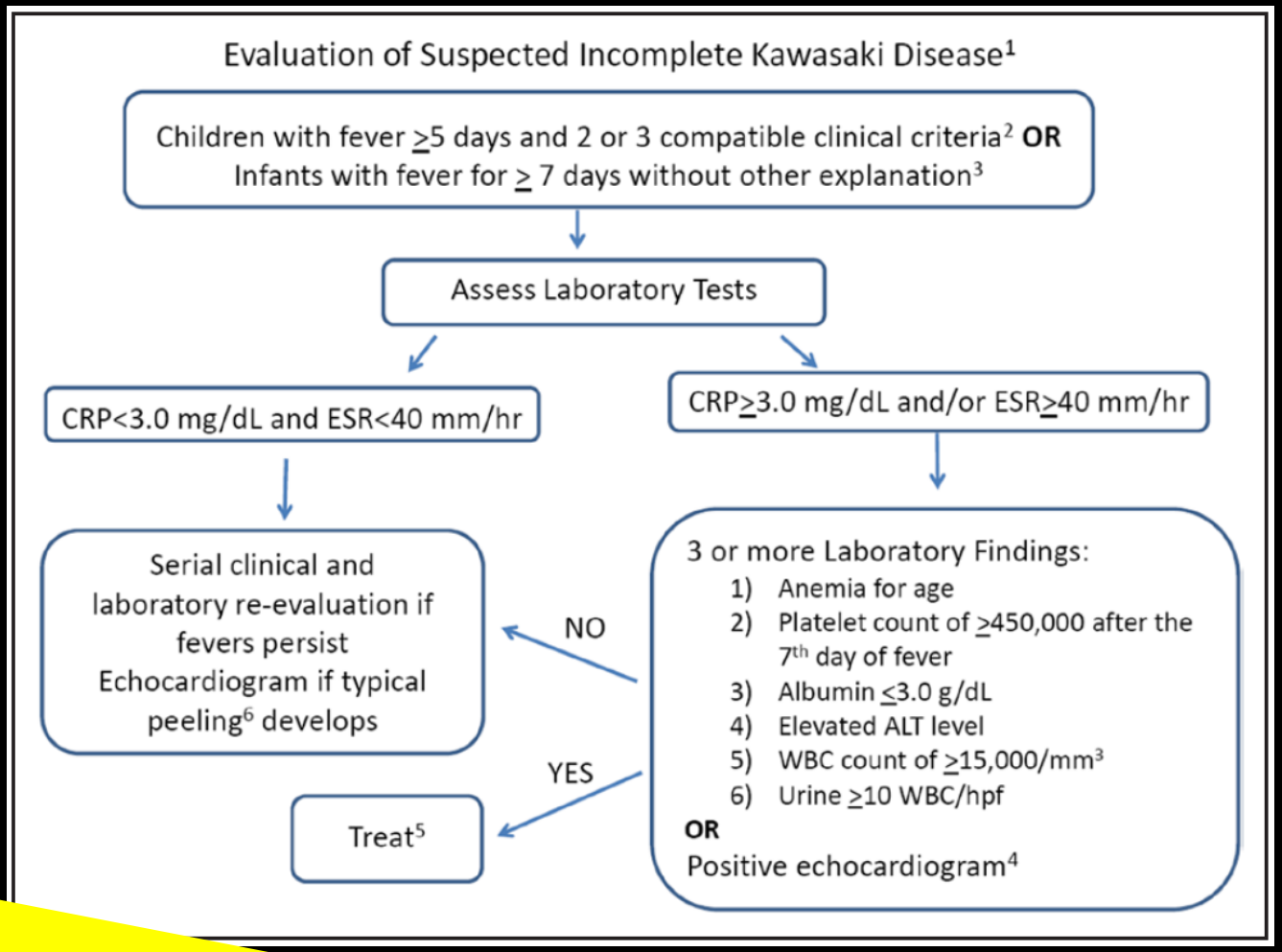

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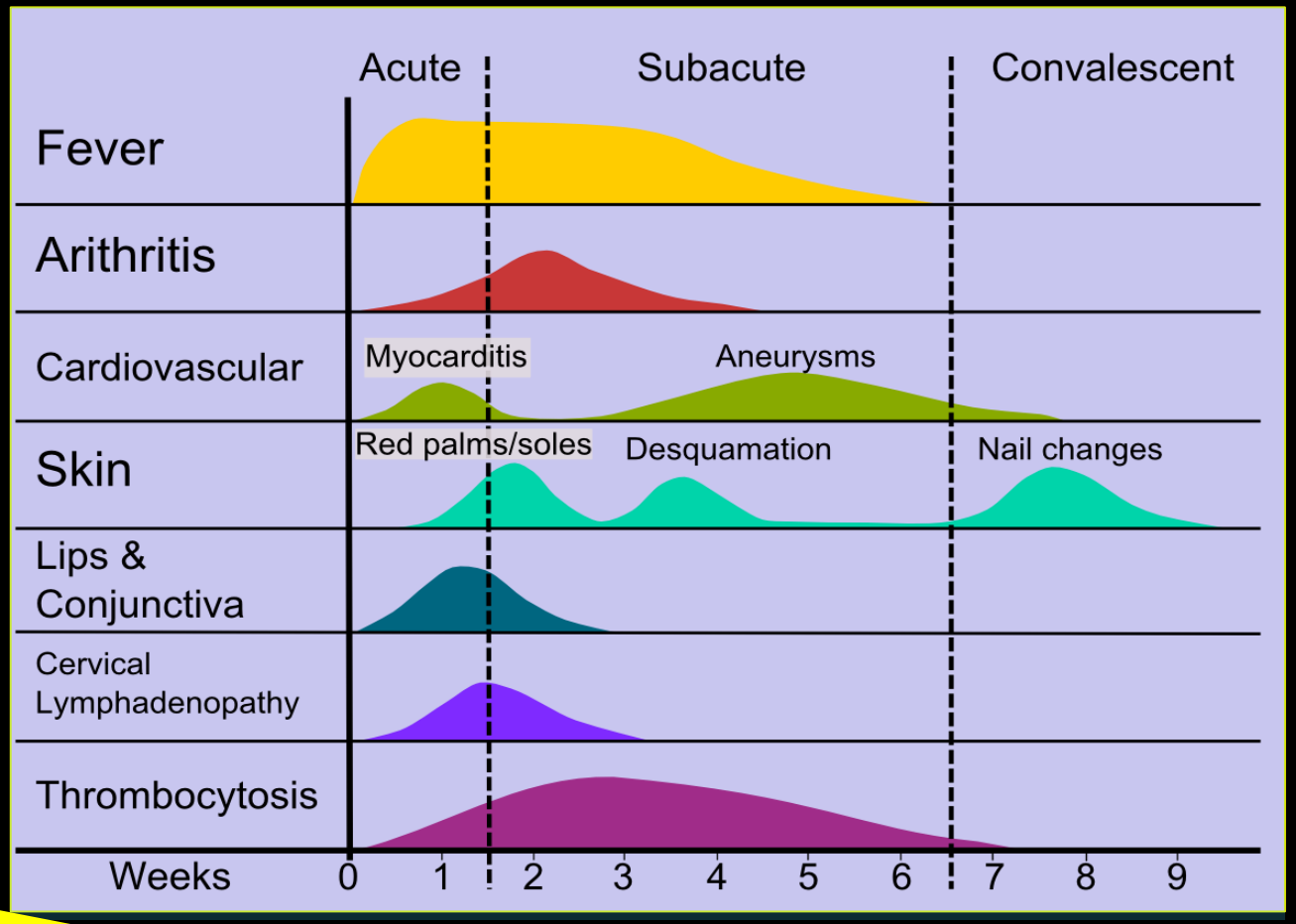

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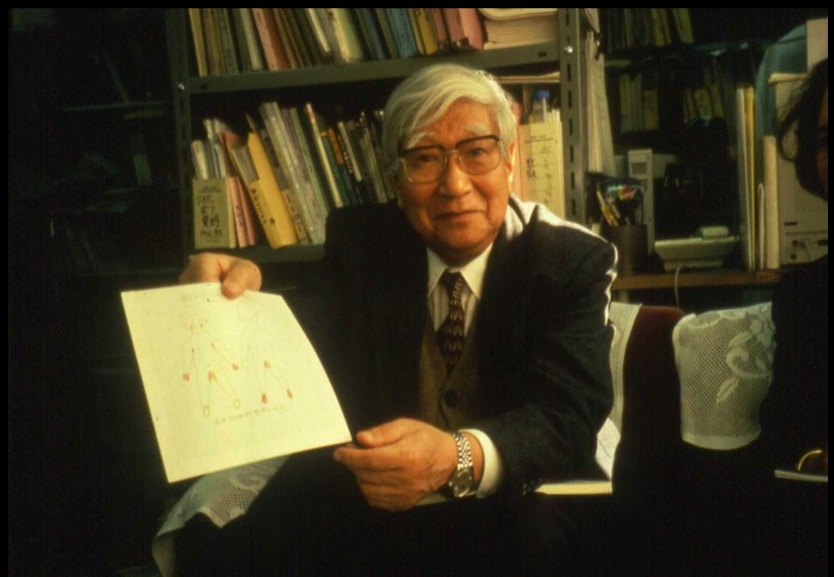

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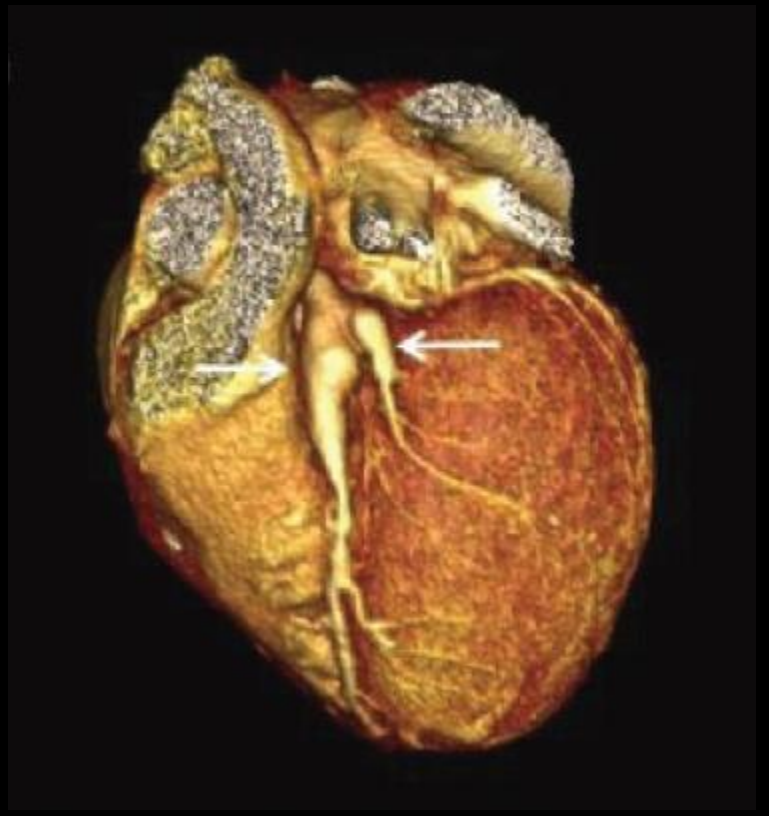
Kawasaki Sendromuna Bağlı Dev Koroner Anevrizma

Ömer Çiftçi[1], Cem Karadeniz[1], Bilge Aldemir Kocabaş[2], Adem Karbuz[2], Tayfun Uçar[1], Erdal İnce[2], Ercan Tutar[1], Ergin Çiftçi[2], Semra Atalay[1]

ONSEKİZ YILLIK KAWASAKİ HASTALIĞI DENEYİMİMİZ: NADİR SEMPTOM VE BULGULARLA HASTALIĞIN DİĞER YÜZÜ

Bilge Aldemir Kocabaş[1], Adem Karbuz[1], Cem Karadeniz[2], Ömer Çiftçi[2], Halil Özdemir[1], Gökalp Musa Bolkent[3], Tayfun Uçar[2], Ercan Tutar[2], Semra Atalay[2], Suat Fitöz[4], Ergin Çiftçi[1], Erdal İnce[1]



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KAWASAKİ HASTALIĞI
Klinik Bulgular

Nervous system
Extreme irritability
Aseptic meningitis (pleocytosis of cerebrospinal fluid)
Facial nerve palsy
Sensorineural hearing loss
Genitourinary
Urethritis/meatitis, hydrocele
Other
Desquamating rash in groin
Retropharyngeal phlegmon
Anterior uveitis by slit lamp examination
Erythema and induration at BCG inoculation site

Other clinical findings may include the following:
Cardiovascular
Myocarditis, pericarditis, valvular regurgitation, shock
Coronary artery abnormalities
Aneurysms of medium-sized noncoronary arteries
Peripheral gangrene
Aortic root enlargement
Respiratory
Peribronchial and interstitial infiltrates on CXR
Pulmonary nodules
Musculoskeletal
Arthritis, arthralgia (pleocytosis of synovial fluid)
Gastrointestinal
Diarrhea, vomiting, abdominal pain
Hepatitis, jaundice
Gallbladder hydrops
Pancreatitis

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Laboratuvar Bulguları

Lökositoz
Nötrofil hakimiyeti
C-reaktif protein artışı
Eritrosit sedimantasyon hızı yüksekliği
Hemoglobin düşüklüğü
Sodyum düşüklüğü
Albümin düşüklüğü
Karaciğer enzimlerinde yükselme
Bilirübin yüksekliği

Steril piyüri
Trombositoz **Ateş başlangıcından sonraki ikinci haftada**

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KAWASAKİ HASTALIĞI

Ayırıcı Tanı

Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

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KAWASAKİ HASTALIĞI

Ayırıcı Tanı

Solunum sinsityal virüsü
Metapneumovirüs
Coronavirüs
İnfluenza virüs
Parainfluenza virüs
...
Klinik bulguları klasik Kawasaki hastalığı ile uyumlu olan bir çocukta tanıyı dışlamaz.

Adenovirüs

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KAWASAKİ HASTALIĞI
Tedavi

IVIG

2 g/kg, 10-12 saat infüzyon

Asetil salisilik asit

80-10 mg/kg/gün
30-50 mg/kg/gün
Ateş 48-72 saat düşene kadar veya 14 gün

3-5 mg/kg/gün, 6-8 hafta

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KAWASAKİ HASTALIĞI
IVIG Dirençli Vakalarda Tedavi

Agent	Description	Dose
Most frequently administered		
IVIG: Second infusion	Pooled polyclonal IG	2 g/kg IV
IVIG + prednisolone	IVIG + steroid	IVIG: 2 g/kg IV + prednisolone 2 $mg \cdot kg^{-1} \cdot d^{-1}$ IV divided every 8 h until afebrile, then prednisone orally until CRP normalized, then taper over 2–3 wk
Infliximab	Monoclonal antibody against TNF-α	Single infusion: 5 mg/kg IV given over 2 h
Alternative treatments		
Cyclosporine	Inhibitor of calcineurin-NFAT pathway	IV: 3 $mg \cdot kg^{-1} \cdot d^{-1}$ divided every 12 h PO: 4–8 $mg \cdot kg^{-1} \cdot d^{-1}$ divided every 12 h Adjust dose to achieve trough 50–150 ng/mL; 2-h peak level 300–600 ng/mL
Anakinra	Recombinant IL-1β receptor antagonist	2–6 $mg \cdot kg^{-1} \cdot d^{-1}$ given by subcutaneous injection
Cyclophosphamide	Alkylating agent blocks DNA replication	2 $mg \cdot kg^{-1} \cdot d^{-1}$ IV
Plasma exchange	Replaces plasma with albumin	Not applicable

IVIG resistance is defined as persistent or recrudescent fever at least 36 hours and <7 days after completion of first IVIG infusion.

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KAWASAKİ HASTALIĞI
Tomisaku Kawasaki

It was in January 1961 that I encountered a child patient, aged 4 years and 3 months, who was to become the first known case of Kawasaki disease. Fifty years have elapsed since then. At the time, I had no choice but to discharge the patient as "diagnosis unknown." Fortunately, the child suffered no sequelae, and is currently enjoying a full and active life as an adult. Since then the incidence of Kawasaki disease has continued to grow. Why? Why can't we stop this disease? The reason, unfortunately, is that its cause is not known. At the time I first described the disease, I felt that we were on the threshold of discovering its cause, since its symptoms were extremely clear-cut. Despite the efforts of numerous researchers, however, we are still searching. It is my strong hope that young researchers will be able to identify the root cause of this disease.

Tomisaku Kawasaki

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KAWASAKİ HASTALIĞI
Tomisaku Kawasaki

In the 2012 interview, Dr. Kawasaki speculated on why distinct cases of the new disease began to emerge in the 1960s. “Probably the use of measles vaccine made it easier to recognize cases of this new entity,” he said, “because measles cases became less common in the population.”

Dr. Tomisaku Kawasaki, Who Pinpointed a Mysterious Disease, Dies at 95

In 1967, he identified a disease that causes heart inflammation in children, one that Covid-19 has brought back into the news.

Dr. Tomisaku Kawasaki in an undated photo. He identified a multisymptom inflammatory syndrome among children that some researchers thought may have been linked to exposure to the new coronavirus.
Agence France-Presse — Getty Images

By Neil Genzlinger

June 17, 2020

Dr. Tomisaku Kawasaki, who in 1967 first identified a disease in children that remains mysterious today and that has recently been in the news in relation to Covid-19, died on June 5 in Tokyo. He was 95.

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COVID-19
Yeni Ortaya Çıkan Enfeksiyon Hastalığı

Çocuklarda
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COVID-19
Yeni Ortaya Çıkan Enfeksiyon Hastalığı

SARA GIRONI CARNEVALE

Scientists are drowning in COVID-19 papers. Can new tools keep them afloat?

By **Jeffrey Brainard** | May. 13, 2020 , 12:15 PM

***Science*'s COVID-19 reporting is supported by the Pulitzer Center.**

Timothy Sheahan, a virologist studying COVID-19, wishes he could keep pace with the growing torrent of new scientific papers about the disease and the novel coronavirus that causes it. But there are just too many—more than 4000 alone last week. "I'm not keeping up," says Sheahan, who works at the University of North Carolina, Chapel Hill. "It's impossible."

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COVID-19
Yeni Ortaya Çıkan Enfeksiyon Hastalığı

Why is COVID-19 so mild in children?

COVID-19 in Newborns and Infants—Low Risk of Severe Disease: Silver Lining or Dark Cloud?

Additional hypotheses about why COVID-19 is milder in children than adults

The immune system of children: the key to understanding SARS-CoV-2 susceptibility?

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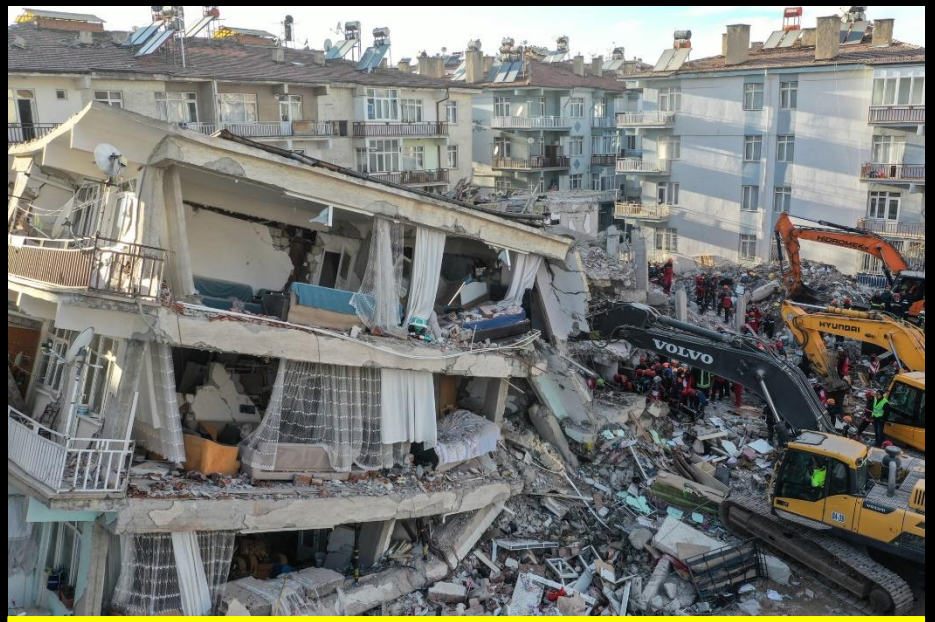
COVID-19
Yeni Ortaya Çıkan Enfeksiyon Hastalığı



COVID-19

MIS-C

Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

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MIS-C
Ortaya Çıkışı

Nisan 2020'de İngiltere'de ve Avrupa'da yeni enfeksiyon hastalığı

- **Ateş**
- **İnflamasyon**
- **Gastrointestinal belirtiler**
- **Multiorgan tutulumu**

- **Kardiyak disfonksiyon, inotrop ihtiyacı**

İtalya'da Kawasaki hastalığı tanısında 30 kat artış

Prof. Dr. Ergin ÇİFTÇİ
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MULTISYMPTOM INFLAMMATORY SYNDROME IN CHILDREN

- FEVER
- LAB EVIDENCE OF INFLAMMATION
- HOSPITALIZATION
- INVOLVEMENT OF MORE THAN 2 ORGAN SYSTEMS
- NO OTHER POSSIBLE DIAGNOSIS

Table 3. CDC Case Definition for MIS-C

Criteria

- An individual aged < 21 years presenting with fever[a], laboratory evidence of inflammation[b], and evidence of clinically severe illness requiring hospitalization, with multisystem (≥ 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological); **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 the 4 weeks prior to the onset of symptoms

[a]Fever > 38.0°C for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours
[b]Including, but not limited to, 1 or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes, and low albumin

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Multisistem İnflamatuvar Sendrom (MIS-C)

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Box. WHO Criteria for MIS-C[a]

Children and adolescents 0 to 19 years old with fever >3 days

AND 2 of the following:

- Rash or bilateral nonpurulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet)
- Hypotension or shock
- Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/NT-proBNP)
- Evidence of coagulopathy (by prothrombin time, partial thromboplastin time, elevated D-dimer levels)
- Acute gastrointestinal symptoms (diarrhea, vomiting, or abdominal pain)

AND elevated markers of inflammation such as erythrocyte sedimentation rate, C-reactive protein level, or procalcitonin level

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

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

Abbreviations: COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children; NT-proBNP, N-terminal pro–brain natriuretic peptide; RT-PCR, reverse transcriptase–polymerase chain reaction; WHO, World Health Organization.

[a] Based on WHO criteria.[18]

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Multisistem İnflamatuvar Sendrom (MIS-C)

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MIS-C
Patogenez

Neden geliştiği belirsiz...

- SARS-CoV-2 virüs replikasyonunun doğrudan etkisi
- Post-enfeksiyöz immün disregülasyon
- Her iki durumun birlikteliği

Post-enfeksiyöz olma olasılığı daha yüksek görülüyor.

- İmmün modülatör antiinflamatuar tedaviye yanıt
- Anti-viral tedavi olmadan iyileşme
- Enfeksiyondan 4-6 hafta sonra görülmesi
- IgG üretiminin IgM'yi geçtiği dönemde görülmesi
- Çoğu hastada SARS-CoV-2 antikor pozitifliği
- NP viral yükün şiddetli COVID-19'a göre daha düşük olması

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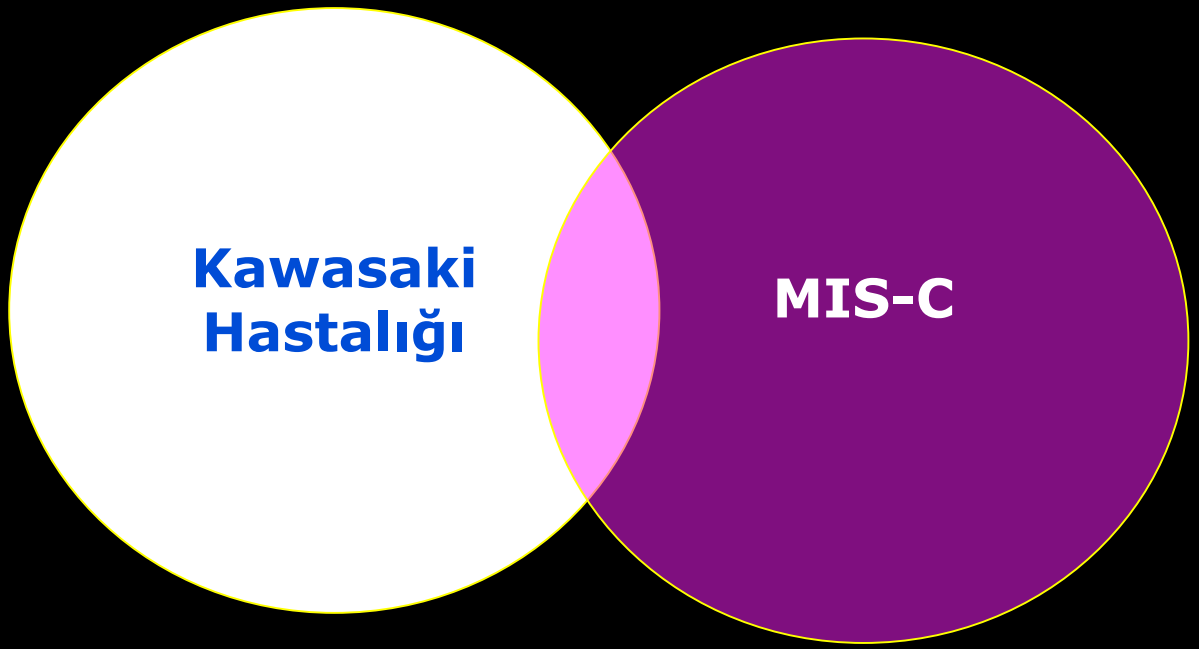
COVID-19 Nerede Başlıyor Nerede Bitiyor?



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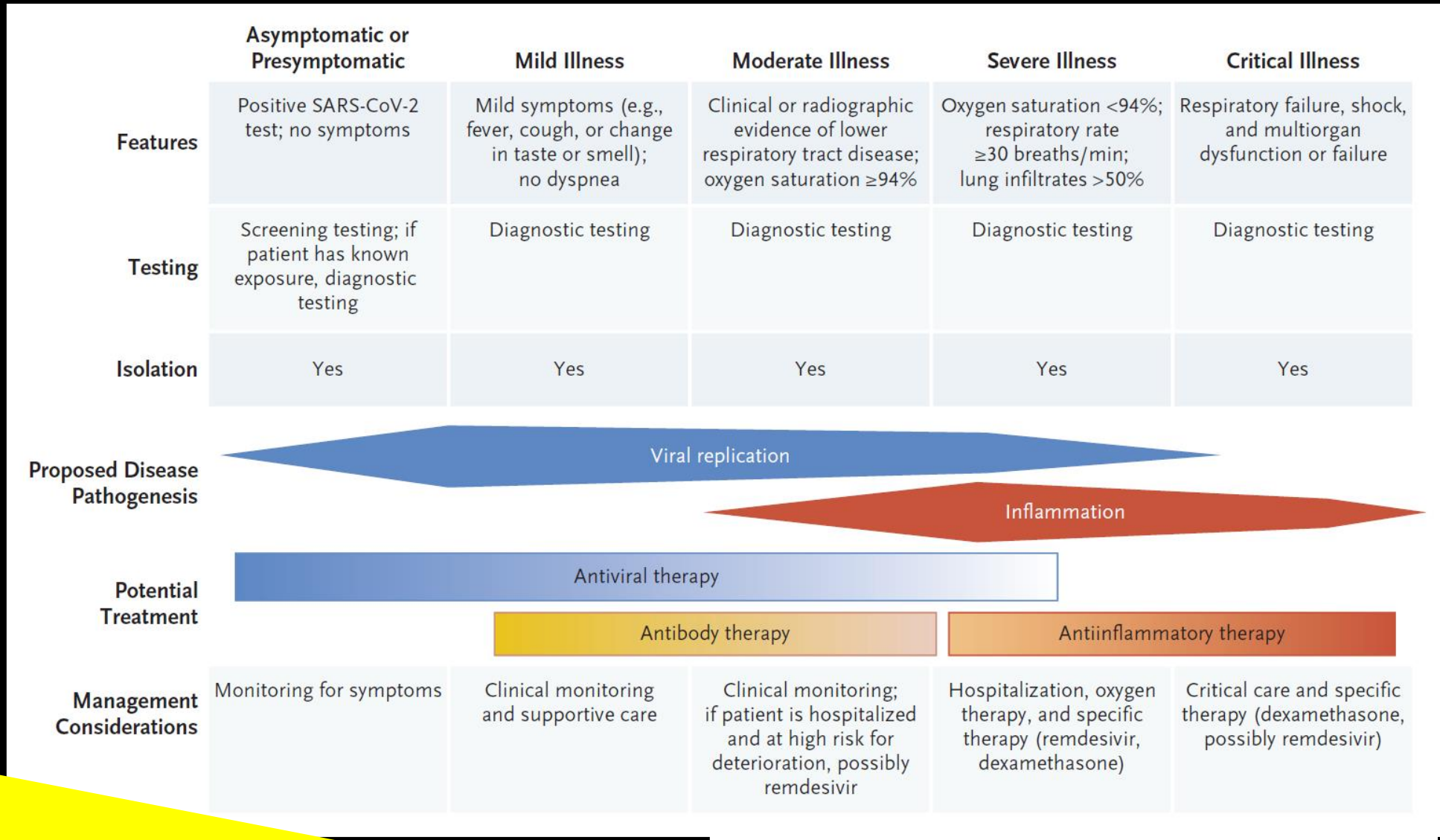

N ENGL J MED 383;18 NEJM.ORG OCTOBER 29, 2020

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Multisistem İnflamatuvar Sendrom (MIS-C)

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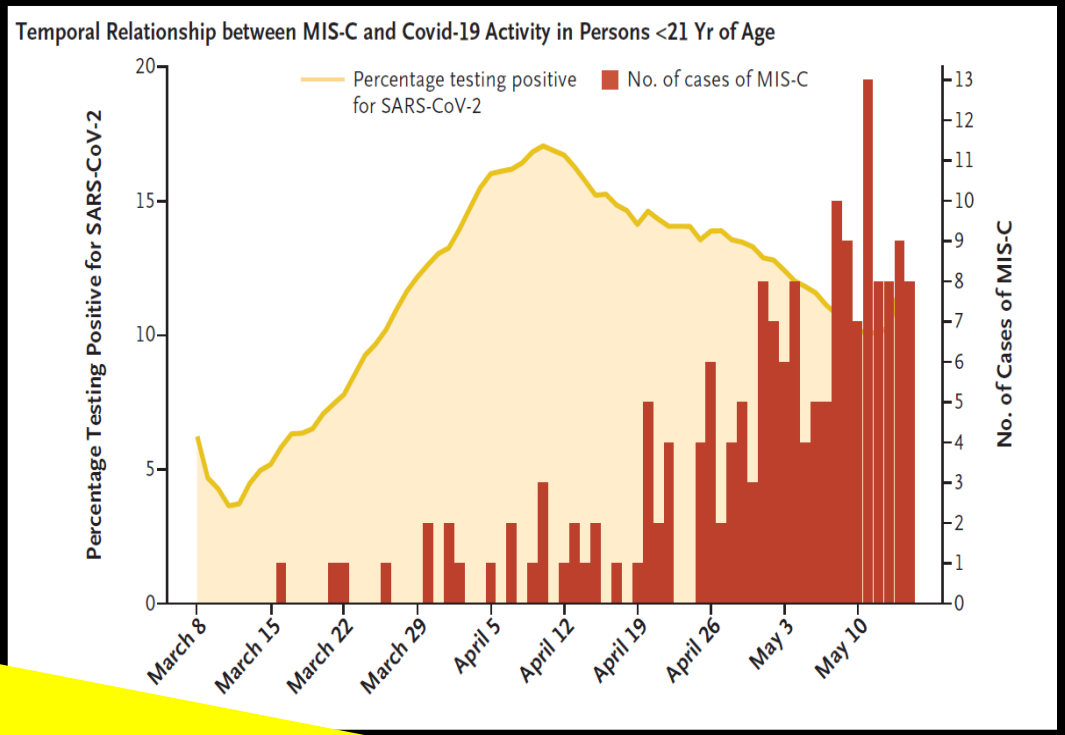
Multisystem Inflammatory Syndrome in U.S. Children and Adolescents

This article was published on June 29, 2020, at NEJM.org.

Çocuk hasta sayısı	**186**
Median yaş	**8.3 yıl**
Mortalite	**%2**
Koroner arter anevrizması	**%8**
Vazoaktif destek	**%48**



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Multisistem İnflamatuvar Sendrom (MIS-C)

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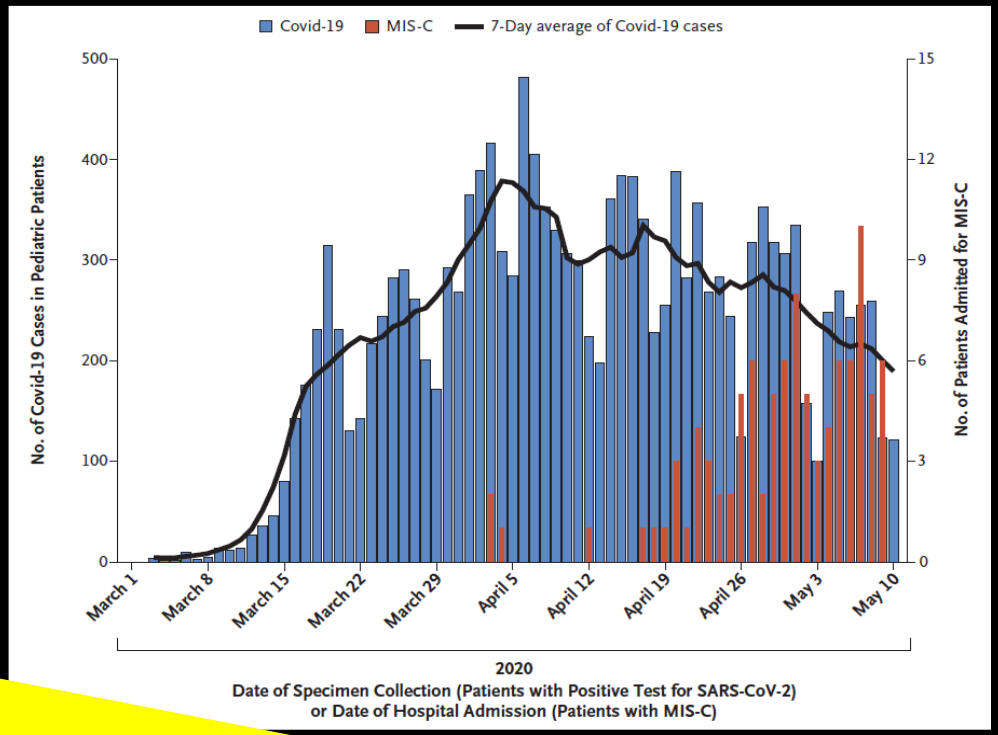
Multisystem Inflammatory Syndrome in Children in New York State

This article was published on June 29, 2020, at NEJM.org.

Çocuk hasta sayısı	**95**
0-5 Yaş %31 6-12 Yaş %42 13-20 Yaş %26	
Mortalite	**%2**
Koroner arter anevrizması	**%9**
Vazoaktif destek	**%61**



Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

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MIS-C
Demografik Özellikler

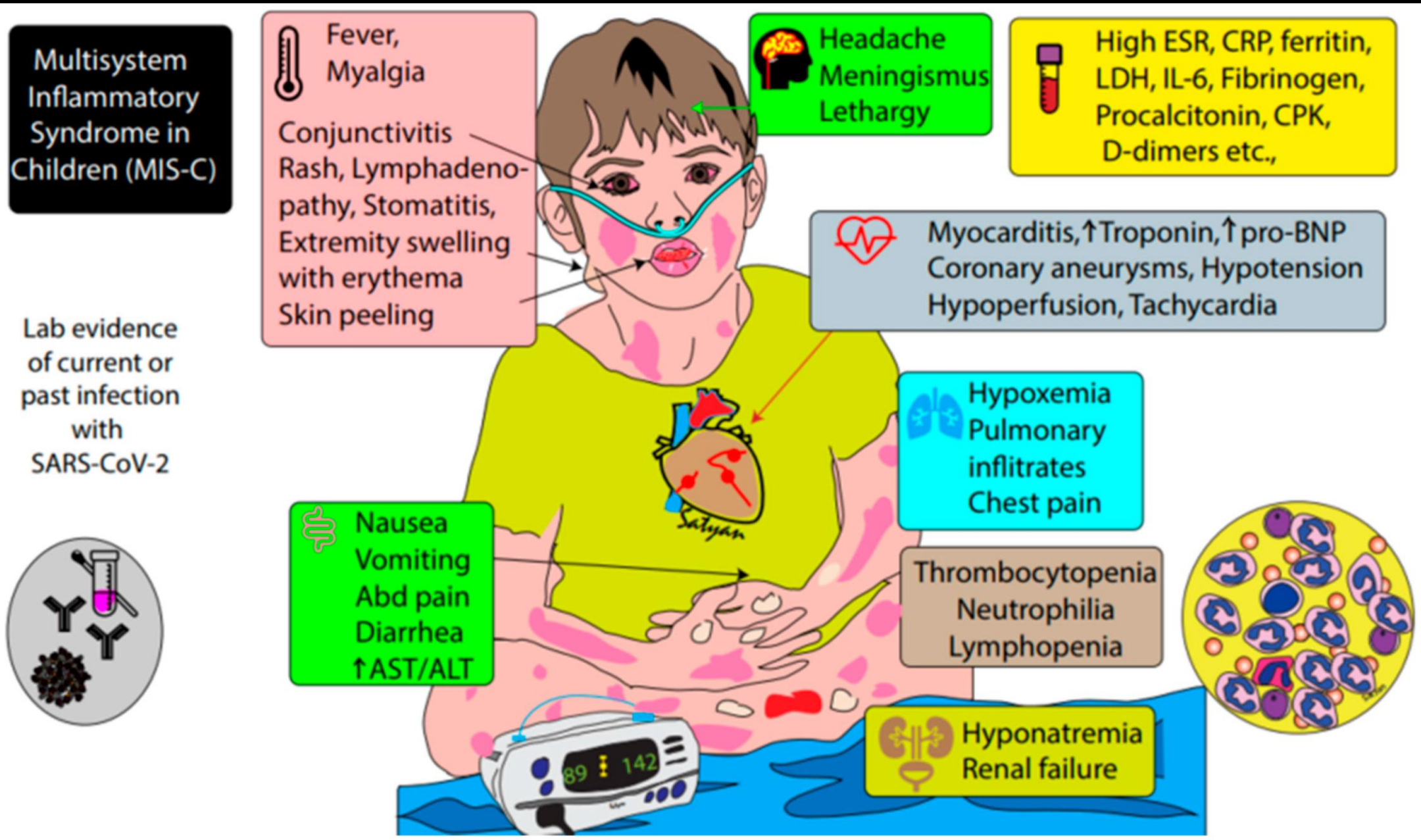
Daha büyük yaştaki çocuklar (median yaş en az 8 yıl, Kawasaki 2 yıl)

Batıda sık, Kore'de nadir, Çin ve Japonya'da neredeyse yok

Erkeklerde daha sık

Obezite en önemli eşlik eden durum

CDC	WHO
Yaş: ❑ <21 yaş **Ateş:** ❑ ≥24 saat > 38.0°C veya ❑ ≥24 saat süren subjektif ateş **Enflamasyonun laboratuar kanıtı:** ❑ CRP ↑, ESR ↑, Fibrinojen ↑, Prokalsitonin ↑, D-dimer ↑, Ferritin ↑, LDH ↑, IL-6 ↑, Nötrofili, Lenfositopeni, Hipoalbüminemi **Multi organ tutulumu : ≥2 organ sistemi:** ❑ KVS: Şok, troponin ↑, BNP ↑, anormal EKO, aritmi ❑ SS: Pnömoni, ARDS, pulmoner emboli ❑ Nefrolojik: ABY ❑ SSS: Nöbet, aseptik menenjit, SVO ❑ Hematolojik: Koagülopati ❑ GİS: Karın ağrısı, kusma, ishal, KCFT ↑, ileus, kanama ❑ Dermatolojik: Eritrodermi, mukozit, diğer döküntüler Hospitalizasyon gerektiren ciddi hastalık **SARS-CoV-2 enfeksiyonu veya teması:** ❑ SARS-CoV-2 RT-PCR + ❑ Seroloji + ❑ Antijen testi + ❑ Semptomların başlamasından önceki 4 haftada COVID-19 teması **Alternatif tanı olmaması**	**Yaş:** ❑ 0-19 yaş **Ateş:** ❑ 3 gün ve üzeri süren ateş **Artmış inflamasyon yanıtı** (ESR, CRP veya prokalsitonin) **Multi organ tutulumu: ≥2** ❑ Döküntü, bilateral nonpürülan konjunktivit veya mukokutanöz inflamasyon (ağız, el/ayaklar) ❑ Hipotansiyon veya şok ❑ Kardiyak disfonksiyon, perikardit, valvülit veya koroner anormallikler (EKO veya troponin / BNP ↑) ❑ Koagülopati varlığı (uzamış PT veya PTT; yüksek D-dimer) ❑ Akut GİS semptomlar (ishal, kusma veya karın ağrısı) **SARS-CoV-2 enfeksiyonunun kanıtı:** Herhangi biri: ❑ SARS-CoV-2 RT-PCR + ❑ Seroloji + ❑ Antijen testi + ❑ COVID-19 olan bir kişiyle temas **Bakteriyel sepsis ve stafilokok/streptokoksik toksik şok sendromları dahil başka mikrobiyal enflamasyon nedeni olmaması**


Multisystem Inflammatory Syndrome in Children (MIS-C)
Fever, Myalgia
Conjunctivitis
Rash, Lymphadeno-pathy, Stomatitis,
Extremity swelling with erythema
Skin peeling
Headache
Meningismus
Lethargy
High ESR, CRP, ferritin, LDH, IL-6, Fibrinogen, Procalcitonin, CPK, D-dimers etc.,
Myocarditis, ↑Troponin, ↑pro-BNP
Coronary aneurysms, Hypotension
Hypoperfusion, Tachycardia
Hypoxemia
Pulmonary inflitrates
Chest pain
Nausea
Vomiting
Abd pain
Diarrhea
↑AST/ALT
Thrombocytopenia
Neutrophilia
Lymphopenia
Hyponatremia
Renal failure
Lab evidence of current or past infection with SARS-CoV-2
89
142

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MIS-C
Tanı

REVIEW

CURRENT OPINION **Multisystem inflammatory syndrome in children**

Vijaya L. Soma[a], Gail F. Shust[a], and Adam J. Ratner[a,b]

Table 1. Reported clinical and laboratory findings in MIS-C

Fever ≥38.0°C for ≥24 h with multisystem (≥2) organ involvement

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Fever ≥38.0°C for ≥24 h with multisystem (≥2) organ involvement
Positive SARS-CoV-2 PCR or serology OR epidemiologic link to a patient with COVID-19

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Multisystem Inflammatory Syndrome in Children (MIS-C) Interim Guidance

What is the case definition of multisystem inflammatory syndrome in children (MIS-C)?

The CDC issued a Health Advisory on May 14, 2020, that outlines the following case definition for MIS-C:

- An individual aged <21 years presenting with fever,[1] laboratory evidence of inflammation,[2] and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological); **AND**
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Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

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MIS-C
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REVIEW

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Fever ≥38.0°C for ≥24 h with multisystem (≥2) organ involvement
Positive SARS-CoV-2 PCR or serology OR epidemiologic link to a patient with COVID-19
Gastrointestinal
Abdominal pain
Nausea/Vomiting
Diarrhea
Cardiovascular
Shock
Hypotension
Congestive heart failure
Myocarditis
Coronary artery dilation/aneurysm
Pericardial effusion
Valvular dysfunction
Elevated troponin
Elevated BNP[1] or NT-proBNP[2]

Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

Clinical Image / *Klinik Görüntü*

DOI: 10.5578/ced.?????? • *J Pediatr Inf 2020;14(4):e???-e???*

Multisystem Inflammatory Syndrome in Children (MIS-C) with COVID-19

COVID-19 İlişkili Çocuklarda Multisistem İnflamatuar Sendromu (MIS-C)

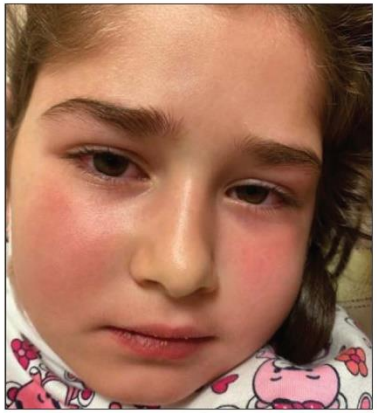
Ergin Çiftçi[1], Gül Arga[1], Esra Çakmak Taşkın[1], Hatice Kübra Konca[1], Halil Özdemir[1]

[1] *Division of Pediatric Infectious Diseases, Department of Pediatrics, Ankara University School of Medicine, Ankara, Turkey*

Cite this article as: Çiftçi E, Arga G, Çakmak Taşkın E, Konca HK, Özdemir H. Multisystem inflammatory syndrome in children (MIS-C) with COVID-19. J Pediatr Inf 2020;14(4):e???-e???.

A seven-year-old girl was brought with complaints of fever, abdominal pain and rash. She was referred to our hospital with acute appendicitis by the hospital she first applied to. It was learned that the girl's grandfather had COVID-19 a month ago. In the examination of the patient, fever was measured as 38.5°C, redness was seen in both conjunctiva and erythema which was more prominent on the cheeks was found on the face. She had cracking and peeling on her lips, a red strawberry tongue appearance, and widespread erythema on her trunk. There was tenderness in the left lower quadrant of the abdomen. Laboratory findings were WBC: 8920/mm^3, Hb: 11.6 g/dL, PLT: 50.000/mm^3. CRP: 93.4 g/L, D-dimer: 8671 ng/mL, ferritin: 289 ng/mL, and albumin: 2.71 g/L. The patient's SARS-CoV-2 PCR was negative, but SARS-CoV-2 antibody was found to be positive. Echocardiography was found to be normal. Multisystem inflammatory syndrome in children (MIS-C) with COVID-19 was considered. The patient received IVIG 2 g/kg as a single dose. Prednisolone 2 mg/kg/d, aspirin 3.5 mg/kg/d, pantoprazole and piperacillin-tazobactam were also started. The patient's fever resolved; all clinical signs regressed. The antibiotic therapy was stopped on the seventh day of her hospitalization, and the patient was discharged with prednisolone tapering in 3 weeks.

Children can usually survive COVID-19 disease without any problems. On the other hand, MIS-C can be seen in some children after infection. Although it was initially thought to have characteristics similar to Kawasaki disease and toxic shock syndromes, it is now accepted as a distinct entity. MIS-C is thought to be an immunological reaction as it occurs weeks after SARS-CoV-2 infection. MIS-C manifests itself in a patient with SARS-CoV-2 exposure history, PCR, antigen or antibody positivity, who has fever, elevated inflammatory markers, and involvement of at least two organ systems (heart, lung, kidney, skin, hematological, gastrointestinal and neurological). However, diseases that may cause a similar clinical picture in patients should be excluded. The disease can be fatal if not recognized and treated appropriately. The prognosis is generally good with IVIG and corticosteroid doses depending on the severity of the disease.



Correspondence Address/Yazışma Adresi
Ergin Çiftçi
Ankara Üniversitesi Tıp Fakültesi,
Çocuk Sağlığı ve Hastalıkları Anabilim Dalı,
Çocuk Enfeksiyon Hastalıkları Bilim Dalı,
Ankara-Türkiye
mail.com

Available Online Date: ??.??.2020

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MIS-C
Tanı

REVIEW

Multisystem inflammatory syndrome in children

Vijaya L. Soma[a], Gail F. Shust[a], and Adam J. Ratner[a,b]

Dermatologic
Rash Mucocutaneous lesions Conjunctival injection Periorbital edema Swollen hands or feet
Hematologic
Elevated D-dimer Thrombocytopenia Lymphopenia
Respiratory
UPPER: Sore throat Congestion LOWER: Cough Shortness of breath Chest tightness/pain Pneumonia Pleural effusion ARDS[3]

Çocuklarda
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MIS-C
Tanı

REVIEW

CURRENT OPINION

Multisystem inflammatory syndrome in children

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Neurologic
Headache Altered mental status/confusion
Renal
Acute kidney injury
Systemic inflammation
Fatigue Weakness Lymphadenopathy Myalgias Elevated CRP[4], ESR[5],fibrinogen, procalcitonin, LDH[6], IL-6[7] Decreased albumin

1. B-type natriuretic peptide; 2. N-terminal (NT)-pro hormone BNP; 3. Acute respiratory distress syndrome; 4. C-reactive protein; 5. Erythrocyte sedimentation rate; 6. Lactate dehydrogenase; 7. Interleukin-6.

Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

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Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

Çocuklarda Görülen COVID-19 İlişkili Multisistem İnflamatuar Sendromu (MIS-C): Olası Diğer Hastalıklar Gözden Kaçırılmamalı

Dilara Beşli Çelik[1], Gül Arga[2], Galip Arıcı[1], Merve Evgin[1], Fatih Bayer[1], Gülçin Bilicen[1], Ahmet Said Özal[1], Hatice Köksal[1], Hatice Kübra Konca[2], Esra Çakmak Taşkın[2], Halil Özdemir[2], Ergin Çiftçi[2]

[1]Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Ankara Üniversitesi Tıp Fakültesi, Ankara, Türkiye
[2]Çocuk Enfeksiyon Hastalıkları Bilim Dalı, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Ankara Üniversitesi Tıp Fakültesi, Ankara, Türkiye

Giriş

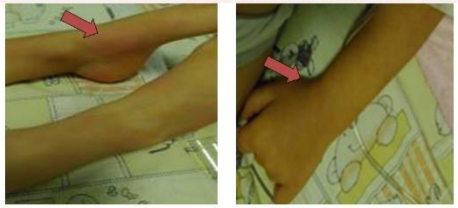
Çocuklarda görülen COVID-19 ilişkili multisistem inflamatuar sendromu (MIS-C) kalp, akciğer, böbrek, deri ile hematolojik, gastrointestinal ve nörolojik sistem tutulumuyla seyreden, geç başlangıçlı, ciddi bir durumdur (Tablo 1). Erken tanı ve tedavi hayati önem taşımaktadır. Bu çalışmada MIS-C tanı kriterlerini karşılayan ancak salmonelloz tanısı alan bir vaka sunulmuş olup, MIS-C'nin bir dışlama tanısı olduğu vurgulanmıştır.

Olgu

Bilinen hastalığı olmayan 4 yaşında kız hasta döküntü, ateş, ishal ve karın ağrısı şikâyetleriyle başvurdu. Ailesinde 1 ay önce geçirilmiş COVID-19 öyküsü olan hastada COVID-PCR, COVID IgM ve IgG negatif olarak sonuçlandı. Muayenesinde alt ekstremitelerinde daha yaygın olmak üzere ekstremite distallerinde eritematöz plak şeklinde, basmakla solan döküntüleri görüldü (Resim 1). Batında hassasiyeti olan hastanın solunum sistemi ve kardiyovasküler sistem muayeneleri doğaldı. Laboratuvarında hemoglobin 10,6 g/dL, lökosit 17.200/mm^3, nötrofil 10.600/mm^3, lenfosit 5400/mm^3, trombosit 472.000/mm^3, CRP 159 mg/L, ESR 72 mm/sa, D-dimer 1263 ng/mL, ferritin 108,6 ng/mL, fibrinojen 7,6 g/L, LDH 326 U/L, albümin 36 g/L iken; kardiyak markerlar normal olarak sonuçlandı. Ekokardiyografide patoloji saptanmadı. Gaita mikroskobisi normaldi. COVID-19 teması olan, gastrointestinal ve cilt tutulumuna D-dimer, ESR ve CRP yüksekliği eşlik eden hastada MIS-C düşünülerek intravenöz immünglobulin (IVIG) 2 g/kg, prednizolon 2 mg/kg/gün, aspirin 3,5 mg/kg/gün ve piperasilin-tazobaktam 400 mg/kg/g tedavileri başlandı. İzleminde ishal nedeniyle gönderilen gaita kültüründe *Salmonella* spp. üredi. Kan kültüründe ise üreme olmadı. Hastanın döküntüsü *Salmonella* için atipik olmakla birlikte, ishali, ateşi ve akut faz reaktanlarında yükseklik olan hastaya salmonelloz tanısı konularak MIS-C tanısı dışlandı. Mevcut tedaviler kesilerek seftriakson 100 mg/kg/gün [illegible]. Hastanın takibinde ishali ve karın ağrısı [illegible]tüleri soldu. Antibiyotiği oral

Tablo 1- MIS-C Vaka Tanımı (Sağlık Bakanlığı COVID-19 Rehberi)

1. 0 - 21 yaş arası	
2. > 24 saat, > 38°C ölçülmüş ateş veya ailenin ateş varlığını bildirimi	
3. Laboratuvar tetiklerinde inflamasyon kanıtı (En az 2 tanesi)	**4. Çoklu organ sistem tutulumu** (En az 2 tanesi)
- Yüksek CRP	- Kardiyovasküler (Şok, yüksek BNP veya troponin, anormal EKO, aritmi)
- Yüksek sedimentasyon	- Solunum (Pnömoni, ARDS, pulmoner emboli)
- Yüksek fibrinojen	- Böbrek (Böbrek yetmezliği)
- Yüksek prokalsitonin	- Nörolojik (Konvülsiyon, inme, aseptik menenjit)
- Yüksek D-dimer	- Hematolojik (Koagülopati, yüksek D-dimer düzeyi)
- Yüksek ferritin	- Gastrointestinal (Yüksek karaciğer enzimleri, diyare, ileus)
- Yüksek LDH	- Dermatolojik (Eritrodermi, mukozit, diğer döküntüler)
- Yüksek IL-6 seviyesi	
- Artmış nötrofil sayısı	
- Lenfositopeni	
- Hipoalbüminemi	
5. Hastaneye yatış gerektirecek ağır hastalık tablosu	
6. Alternatif başka tanı olmaması (Bakteriyel sepsis, enterovirüs enfeksiyonu gibi miyokardit ilişkili enfeksiyonlar, stafilokoksik veya streptokoksik TŞS)	
6. Geçirilmiş veya geçirilmekte olan SARS-CoV-2 enfeksiyonu (En az biri)	
- SARS-CoV-2 RT-PCR pozitifliği	- SARS-CoV-2 antijen pozitifliği
- SARS-CoV-2 seroloji pozitifliği	- Semptomların başlamasından önce 4 hafta içerisinde pozitif olgu teması



Resim 1. Ekstremite distallerinde basmakla solan eritematöz plaklar

Sonuç

COVID-19 ilişkili MIS-C olgu bildirimleri giderek artmaktadır. Mevcut tanı kriterleriyle birçok hastalığın MIS-C tanısı alması olasıdır. MIS-C'nin bir dışlama tanısı olduğu unutulmamalı, benzer tabloya neden olabilecek hastalıklar mutlaka göz önünde bulundurulmalıdır.

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MIS-C
Ayırıcı Tanı

Kesişen özellikleri olan hastalıklar...

- COVID-19
- MIS-C
- Kawasaki hastalığı
- Makrofaj aktivasyon sendromu
- Hemofagositik lenfohistiositoz
- Toksik şok sendromu

Table 2. Differential diagnosis of MIS-C

	MIS-C	KD	TSS	HLH/MAS
Dominantly affected age group	School-age children and adolescents	Infants and toddlers	Any age	Any age
Prolonged fever	Yes	Yes	Yes	Yes
Fissured lips	Common	Typical	Possible	Insufficient data
Nonexudative conjunctivitis	Common	Typical	Possible	Possible
Hypotension	Common	Possible	Typical	Possible
GIS symptoms	Very common	Rare	Common	Rare
Coronary aneurysms	Possible	Common	Insufficient data	Insufficient data
Heart failure	Common	Possible	Rare	Rare
Neutrophilia	Yes	Yes	Yes	No
Lymphopenia	Yes	No	No	Yes
Thrombocytopenia	Yes	No	Yes	Yes
CRP	Elevated	Elevated	Elevated	Elevated
Ferritin	Elevated	Normal, or elevated	Normal	Elevated
Hypertriglyceridemia	Common	No	No	Typical

...ive protein; GIS, gastrointestinal system; HLH/MAS, hemophagocytic lymphohistiocytosis/macrophage activation syndrome; KD, Kawasaki disease; ...atory syndrome in children; TSS, toxic shock syndrome.

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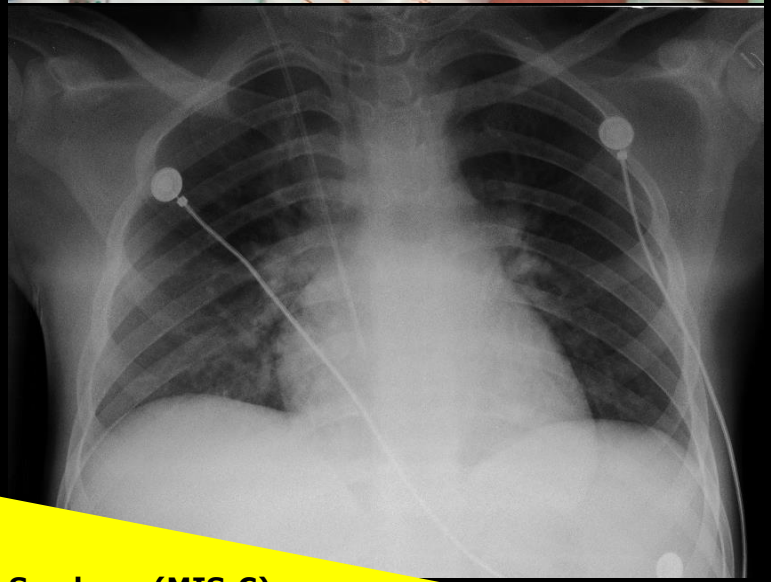

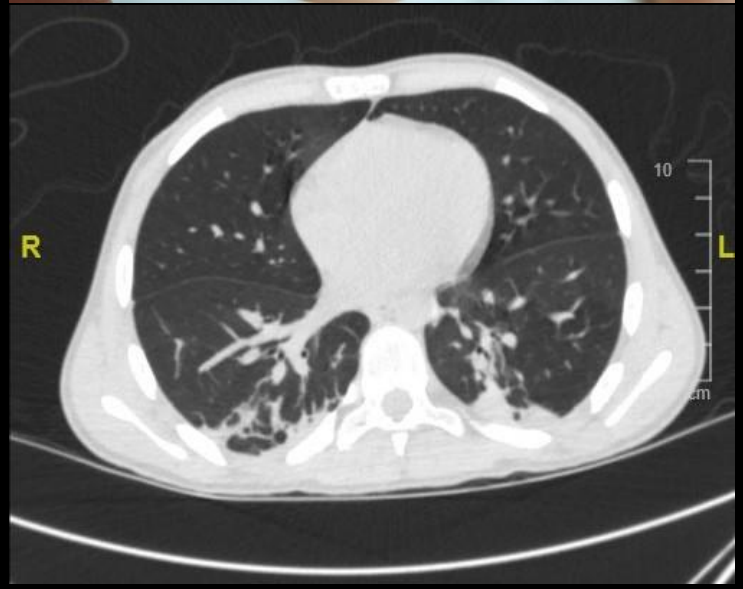

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MIS-C VAKA: 24

Seroloji pozitif : 15
Covid-19 PCR (+) : 3
Klinik : 6 Bilinen Covid-19 PCR (+) ile temas: 3

GIS : 19
Mukokutanöz : 13
Solunum : 10
KVS : 9
Renal : 7
Nörolojik : 2

YBÜ yatış : 9

Tedavi:
- **IVIG : 23**
- **Steroid : 24**
- **ASA : 21**
- **Antikoagülan : 2**
- **Favipiravir : 1**
- **Anakinra : 1**
- **Tosilizumab : 0**

Mortalite : 2

Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

Acute Abdomen—A Clinical Presentation of MIS-C in Children

Emrah Gün[1] Tanıl Kendirli[1] Edin Botan[1] Berrin Demir[2] Ergun Ergün[3] Halil Özdemir[4] Ömer Suat Fitoz[2] Ergin Ciftci[4] Ercan Tutar[5]

J Pediatr Infect Dis 2022;17:24–32.

Abstract

Objective Multisystemic inflammatory syndrome in children (MIS-C) is characterized by persistent fever, systemic hyperinflammation, and multiple-organ dysfunction. There are a few reports about MIS-C presenting with acute abdomen. The aim of this study was to demonstrate the clinical characteristics and treatment options for MIS-C-related acute abdomen and appendicitis.

Methods This was a retrospective study conducted between April 2020 and October 2020 in our pediatric intensive care unit in Turkey. Patients between the ages of 1 month and 18 years who presented with acute abdomen and were ultimately diagnosed with MIS-C were included.

Results Seven patients with a median age of 12.5 (interquartile range 10.5–13) years were enrolled. Four were females. The most frequent symptoms were fever, abdominal pain, and vomiting. Three patients had involvement of the appendix that required surgical intervention. All pathology reports were compatible with appendicitis. The other patients also had an acute abdomen. One patient had malignant hyperthermia during induction of anesthesia, so surgery was postponed and medical management was commenced. The clinical picture regressed with immunomodulation. All patients were treated with intravenous immunoglobulin and steroids. Four patients with acute abdomens improved with immunomodulation, and surgery was not needed.

Conclusion MIS-C may present with an acute abdomen. Immunomodulation should be considered instead of surgery if the clinical course is not complicated.

Keywords

- multisystem inflammatory syndrome in children
- COVID-19
- intestinal inflammation
- appendicitis
- children

Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

Multisystem Inflammatory Syndrome in Children Admitted to a Tertiary Pediatric Intensive Care Unit

Emrah Gün[1] Tanıl Kendirli[1] Edin Botan[1] Nazmiye Türker[2] Anar Gurbanov[1] Burak Balaban[1] Ali Genco Gencay[1] Gül Arga[3] Selen Karagözlü[4] Mehmet Gökhan Ramoglu[4] Halil Özdemir[3] Tayfun Ucar[4] Ercan Tutar[4] Ergin Ciftci[3]

J Pediatr Intensive Care 2023;12:37–43.

Abstract

Background Multisystem inflammatory syndrome in children (MIS-C) is characterized by persistent fever, abdominal pain, vomiting, diarrhea, rash, conjunctivitis, headaches, and mucocutaneous manifestations and it can cause circulatory dysfunction, resulting in hypotension, shock, and end-organ injury in the heart and other organs and possibly death. In this study, we aimed to analyze the clinical spectrum, treatment options and outcomes of children with MIS-C who were admitted to our pediatric intensive care (PICU).

Materials and Methods Clinical and laboratory findings and treatment of the patients admitted to the PICU with MIS-C between April 2020 and January 2021 were recorded, and their outcomes were evaluated.

Results Nineteen patients with a median age of 12.5 years (interquartile range (IQR): 5.8–14.0 years) were admitted. Eleven (57.8%) were males. The most frequent clinical and laboratory features were fever (100%), abdominal pain (94.7%), rash (63.1%), headache (68.4%), diarrhea (47.3%), seizure (10.5%), cardiac dysfunction (52.6%), acute kidney injury (26.3%), lymphopenia (84.2%), and thrombocytopenia (36.8%). However, 8 patients needed mechanical respiratory support, 11 patients needed inotropes, 2 patients needed plasma exchange, and 1 patient needed continuous renal replacement therapy. All patients received corticosteroids, 17 patients (89.2%) received intravenous immunoglobulin, 2 patients received anakinra, 10 patients received acetylsalicylic acid, and 6 patients received enoxaparin. Median PICU length of stay was 3 days (IQR: 2–5) and only one patient died.

Conclusion In conclusion, MIS-C may present with a variety of clinical manifestations, and it can lead to life-threatening critical illness. Most children need intensive care and the response to immunomodulation is usually favorable.

Keywords

- multisystem inflammatory syndrome in children
- COVID-19
- children
- pediatric intensive care

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COVID-19 associated multisystemic inflammatory syndrome in 614 children with and without overlap with Kawasaki disease-Turk MIS-C study group

Dilek Yilmaz Ciftdogan[1,2] · Yildiz Ekemen Keles[2] · Benhur Sirvan Cetin[3] · Nazan Dalgic Karabulut[4] · Melike Emiroglu[5] · Zafer Bagci[6] · Ayse Buyukcam[7] · Emine Hafize Erdeniz[8] · Gul Arga[9] · Edanur Yesil[10] · Ozlem Cakici[11] · Adem Karbuz[12] · Zumrut Sahbudak Bal[13] · Soner Sertan Kara[14] · Arife Ozer[15] · Ozge Metin Akcan[16] · Sefika Elmas Bozdemir[17] · Ayse Berna Anil[1] · Hatice Uygun[18] · Omer Kilic[19] · Selda Hancerli Torun[20] · Zuhal Umit[21] · Murat Sutcu[22] · Berfin Ozgokce Ozmen[23] · Hatice Karaoglu Asrak[24] · Gulsum Alkan[5] · Ahu Kara Aksay[2] · Cuneyt Ugur[6] · Ahmet Ziya Birbilen[7] · Burcu Bursal Duramaz[25] · Esra Akyuz Ozkan[8] · Ozgur Burakay[11] · Sema Yildirim Arslan[13] · Eda Karadag Oncel[2] · Serkan Fazli Celik[14] · Ahmet Osman Kilic[16] · Seval Ozen[18] · Remzi Sarikaya[15] · Demet Demirkol[20] · Gazi Arslan[24] · Ozden Turel[25] · Ahmet Sert[5] · Ergul Sari[26] · Zerrin Orbak[27] · Irfan Oguz Sahin[8] · Celal Varan[18] · Hacer Akturk[28] · Sadiye Kubra Tuter Oz[5] · Fatih Durak[7] · Mehmet Burhan Oflaz[16] · Manolya Kara[22] · Derya Karpuz[23] · Mey Talip Petmezci[12] · Nevin Hatipoglu[26] · Selim Oncel[11] · Mehmet Turgut[18] · Ferhan Elmali[1] · Ayper Somer[20] · Necdet Kuyucu[23] · Ener Cagri Dinleyici[19] · Zafer Kurugöl[13] · Ergin Ciftci[9] · Ates Kara[29]

European Journal of Pediatrics (2022) 181:2031–2043

What is New:

- *Half of the patients had clinical features that overlapped with Kawasaki disease.*
- *In patients whose clinical features overlapped with KD, procalcitonin levels were almost 15 times higher than normal.*
- *Lethargy increased the risk of overlap with KD by 2.6-fold in MIS-C patients.*
- *Transient bradycardia was noted in approximately 10% of our patients after initiation of treatment.*

Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

Multisystem inflammatory syndrome in children associated with COVID-19 in 101 cases from Turkey (Turk-MISC study)

Dilek Yilmaz Ciftdogan,[1,2] Yildiz Ekemen Keles,[2] Adem Karbuz,[3] Benhur Sirvan Cetin,[4] Sefika Elmas Bozdemir,[5] Eda Kepenekli Kadayifci,[6] Ozge Metin Akcan,[7] Arife Ozer,[8] Tugba Erat,[9] Murat Sutcu,[10] Ayse Buyukcam,[11] Nursen Belet,[12] Emine Hafize Erdeniz,[13] Nazan Dalgic Karabulut,[14] Selda Hancerli Torun,[15] Selim Oncel,[16] Zerrin Orbak,[17] Ozden Turel,[18] Zeynep Gokce Gayretli Aydin,[19] Omer Kilic,[20] Aysun Yahsi,[21] Ahu Kara Aksay,[2] Zeynep Ergenc,[6] Mey Talip Petmezci,[22] Mehmet Burhan Oflaz,[23] Remzi Sarikaya,[24] Gülcin Otar Yener,[25] Seval Ozen,[26] Doruk Gul,[27] Gazi Arslan,[28] Soner Sertan Kara,[29] Demet Demirkol,[30] Pinar Yazici Ozkaya,[31] Yilmaz Yozgat,[32] Celal Varan,[33] Manolya Kara,[34] Gul Arga,[35] Nurhayat Yakut,[6] Ahmet Osman Kilic,[36] Ozlem Cakici,[16] Mehmet Kucuk,[37] Ozge Kaba,[15] Hatice Karaoglu Asrak,[12] Burcu Bursal Duramaz,[18] Tahir Dalkiran,[38] Ayse Berna Anil,[39] Mehmet Turgut,[26] Bulent Karapinar,[31] Ayper Somer,[15] Ferhan Elmali,[40] Ener Cagri Dinleyici,[41] Ergin Ciftci[35] and Ates Kara[42]

Journal of Paediatrics and Child Health **58** (2022) 1069–1078

What is already known on this topic

1 Multisystem inflammatory syndrome in children (MIS-C) occurs in association with SARS-CoV-2 infection and presents with fever, involvement of multiple organ systems and evidence of inflammation.
2 Most patients with MIS-C are diagnosed with serological tests.
3 Unlike classical Kawasaki disease, most patients are over 5 years.

What this paper adds

1 Fever lasted at least 3 days in all patients.
2 Kawasaki-like features were primarily detected in children aged 5 to 12 years.
3 Lymphopenia was predominant over 12 years.
4 Some patients had bradycardia after starting treatment.

Results: The study comprised 101 patients, median age 7 years (interquartile range (IQR) 4.6–9.3); 51 (50.5%) were boys. Reverse-transcriptase polymerase chain reaction (PCR) assay was positive in 21/100 (21%) patients; 62/83 (74.6%) patients had positive serology for SARS-CoV-2. The predominant complaints were fever (100%), fatigue (n = 90, 89.1%), and gastrointestinal symptoms (n = 81, 80.2%). Serum C-reactive protein (in 101 patients, median 165 mg/L; range 112–228), erythrocyte sedimentation rate (73/84, median 53 mm/s; IQR 30–84) and procalcitonin levels (86/89, median 5 μg/L; IQR 0.58–20.2) were elevated. Thirty-eight patients (37.6%) required admission to intensive care. Kawasaki disease (KD) was diagnosed in 70 (69.3%) patients, 40 of whom had classical KD. Most patients were treated with intravenous immunoglobulin (n = 92, 91%) and glucocorticoids (n = 59, 58.4%). Seven patients (6.9%) died.

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Multisystem inflammatory syndrome in children during the COVID-19 pandemic in Turkey: first report from the Eastern Mediterranean

Yasemin Ozsurekci[1] · Sibel Gürlevik[1] · Selman Kesici[2] · Ummusen Kaya Akca[3] · Pembe Derin Oygar[1] · Kubra Aykac[4] · Dilek Karacanoglu[2] · Ozlem Sarıtas Nakip[2] · Sare Ilbay[1] · Ban Katlan[2] · İlker Ertugrul[5] · Ali Bülent Cengiz[1] · Ozge Basaran[3] · Burcu Ceylan Cura Yayla[4] · Jale Karakaya[6] · Yelda Bilginer[3] · Benan Bayrakci[2] · Mehmet Ceyhan[1] · Seza Ozen[3]

Received: 2 January 2021 / Revised: 31 January 2021 / Accepted: 2 February 2021

Abstract

Objective We aimed to describe the typical clinical and laboratory features and treatment of children diagnosed with multisystem inflammatory syndrome in children (MIS-C) and to understand the differences as compared to severe/critical pediatric cases with COVID-19 in an eastern Mediterranean country.

Methods Children (aged <18 years) who diagnosed with MIS-C and severe/critical pediatric cases with COVID-19 and were admitted to hospital between March 26 and November 3, 2020 were enrolled in the study.

Results A total of 52 patients, 22 patients diagnosed with COVID-19 with severe/critical disease course and 30 patients diagnosed with MIS-C, were included in the study. Although severe COVID-19 cases and cases with MIS-C share many clinical and laboratory features, MIS-C cases had longer fever duration and higher rate of the existence of rash, conjunctival injection, peripheral edema, abdominal pain, altered mental status, and myalgia than in severe cases ($p<0.001$ for each). Of all, 53.3% of MIS-C cases had the evidence of myocardial involvement as compared to severe cases (27.2%). Additionally, C-reactive protein (CRP) and white blood cell (WBC) are the independent predictors for the diagnosis of MIS-C, particularly in the existence of conjunctival injection and rash. Corticosteroids, intravenous immunoglobulin (IVIG), and biologic immunomodulatory treatments were mainly used in MIS-C cases rather than cases with severe disease course. There were only three deaths among 52 patients, one of whom had Burkitt lymphoma and the two cases with severe COVID-19 of late referral.

Conclusion Differences between clinical presentations, acute phase responses, organ involvements, and management strategies indicate that MIS-C might be a distinct immunopathogenic disease as compared to pediatric COVID-19. Conjunctival injection and higher CRP and low WBC count are reliable diagnostic parameters for MIS-C cases.

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Multisystem Infl

Critical Updates on COVID-19 / Clinical Guidance

What is the recommended treatment approach for MIS-C?

Clinicians who suspect MIS-C in a child should use a multidisciplinary approach involving many pediatric specialists, which may include but is not limited to cardiology, infectious disease, immunology, hematology, rheumatology, pediatric hospital medicine, and critical care, to guide individual patient treatment.

- Patients with MIS-C have been treated wit IVIG, 1 to 2 grams/kg; patient cardiac function and fluid status influence timing of IVIG therapy.
- Some patients have also been treated wit steroid therapy (ranging from 2 to 30 mg/kg/day of methylprednisolone depending on severity of illness) and biologics (eg anakinra, 2 to 10 mg/kg/day, subcutaneously or intravenously, divided every 6 to 12 hours). If the patient has laboratory or imaging evidence of myocarditis or findings concerning for coronary artery aneurysms, discussion with pediatric cardiology is suggested prior to use of steroids.
- Patients treated with steroids and/or biologics often go home with a 3-week taper of steroids and/or biologics.
- Given the need for early intervention and the need to initiate treatment for multiple possible etiologies, many patients have received concurren antibiotic therapy.
- Assessment of clotting risk and need for treatment/prophylaxis is recommended (eg, low-dose aspirin, at a minimum, for patients with Kawasaki disease-like syndrome c enoxaparin i patients with thrombosis). Specialists involved may include cardiology and/or hematology.

- fluid resuscitation;
- inotropic support;
- respiratory support; and
- in rare cases, extracorporeal membranous oxygenation (ECMO).

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Multisystem Inflammatory Syndrome in Children (MIS-C) Interim Guidance

What is the recommended follow-up for MIS-C patients?

Patients diagnosed with MIS-C should have close outpatient pediatric cardiology follow-up starting 2 to 3 weeks after discharge. Patients diagnosed with myocarditis should have cardiology directed restriction and/or release for vigorous activities.

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Cardiac management of MIS-C:

- Patients with MIS-C and abnormal BNP and/or troponin T at diagnosis should have these laboratory parameters trended over time until they normalize (H).
- EKGs should be performed at a minimum of every 48 hours in MIS-C patients who are hospitalized and during follow-up visits. If conduction abnormalities are present, patients should be placed on continuous telemetry while in the hospital, and Holter monitors should be considered during follow-up (M/H).
- Echocardiograms conducted at diagnosis and during clinical follow-up should include evaluation of ventricular/valvar function, pericardial effusion, and coronary artery dimensions with measurements indexed to body surface area using z-scores (H).
- Echocardiograms should be repeated at a minimum of 7-14 days and 4-6 weeks after presentation. For those patients with cardiac abnormalities occurring in the acute phase of their illness, an echocardiogram 1 year after MIS-C diagnosis could be considered. Patients with left ventricular (LV) dysfunction and/or CAA will require more frequent echocardiograms (M/H).
- Cardiac MRI may be indicated 2-6 months after MIS-C diagnosis in patients who presented with significant transient LV dysfunction in the acute phase of illness (LV ejection fraction <50%) or persistent LV dysfunction. Cardiac MRI should focus on myocardial characterization including functional assessment, T1/T2 weighted imaging, T1 mapping and extracellular volume (ECV) quantification, and late gadolinium enhancement (H).
- Cardiac CT should be performed in patients with suspicion of distal CAAs that are not well seen on echocardiogram (M).

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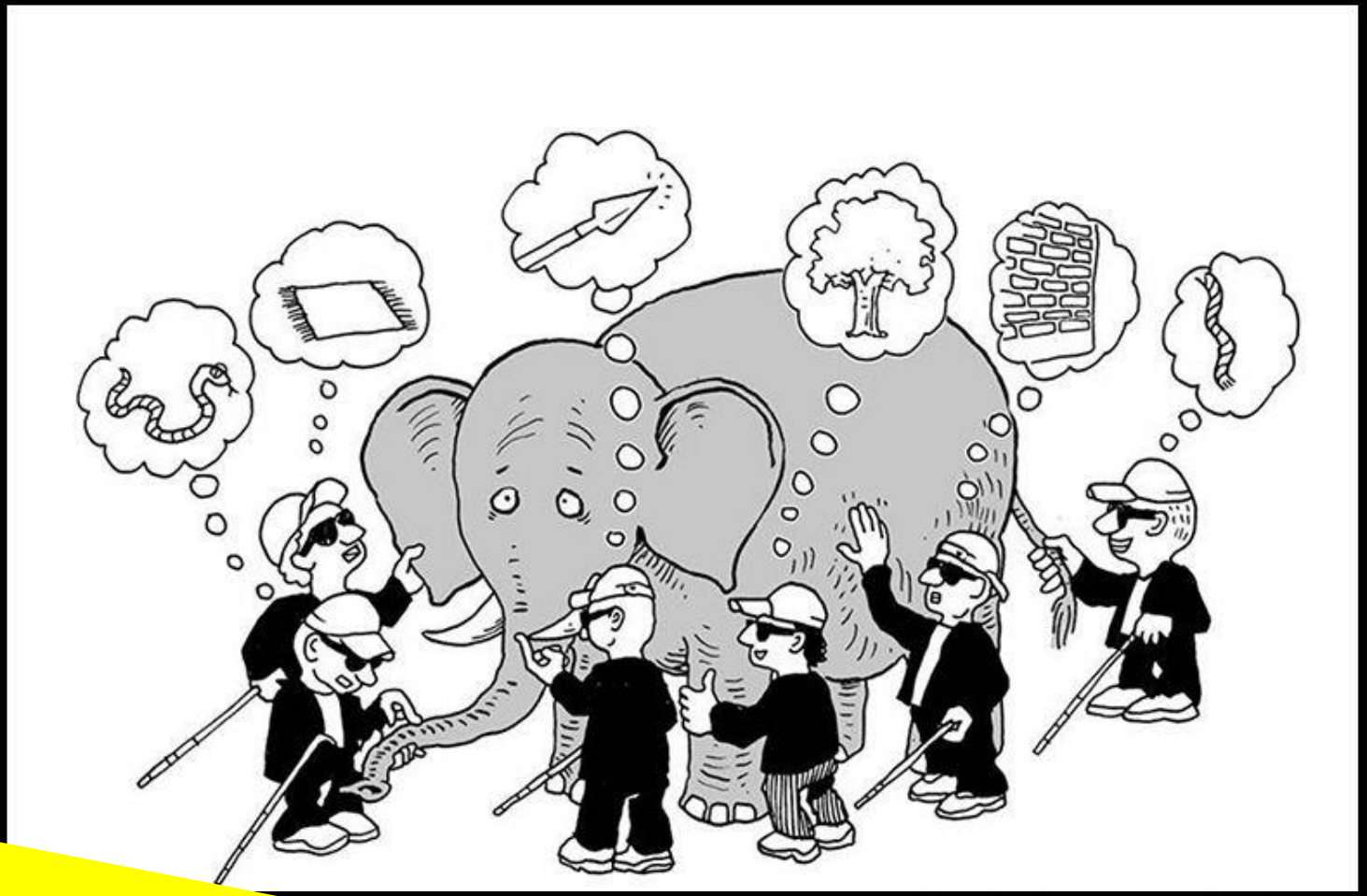
MIS-C
Tam Olarak Nedir?



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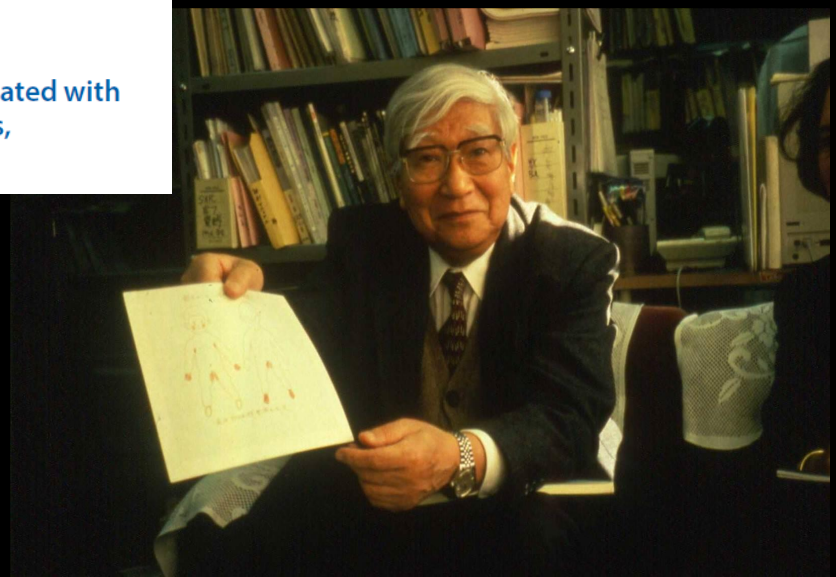
MIS-C
Tam Olarak Nedir?

Multisystem inflammatory syndrome in children (MIS-C) and neonates (MIS-N) associated with COVID-19: optimizing definition and management

Morbidity and Mortality Weekly Report

Case Series of Multisystem Inflammatory Syndrome in Adults Associated with SARS-CoV-2 Infection — United Kingdom and United States, March–August 2020



Çocuklarda
Multisistem İnflamatuvar Sendrom (MIS-C)

Prof. Dr. Ergin ÇİFTÇİ
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MIS-C
Buzdağının Altında Neler Var?

Jolyon Attwooll

10 Jun 2022

‘Significant’ drop in MIS-C risk under Omicron: study

Vaccination also looks to be confirmed as a factor in reducing the risk of complications in children after COVID-19 infection, according to new research.

There have been more than 100 cases of MIS-C in Australia so far.

Omicron causes far fewer cases of multisystem inflammatory syndrome in children (MIS-C), a new study from Denmark suggests.

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