Case Report / Olgu Sunumu

DOI: 10.4274/cayd.galenos.2022.25743
J Pediatr Emerg Intensive Care Med 2023;10:57-61

A Case of Measles Initially Diagnosed as MIS-C in the COVID-19 Pandemics

COVID-19 Pandemisinde MİS-C ile Karışan Bir Kızamık Olgusu

Doğa Lüleyap[1], Ayşe Berna Anıl[2], Pınar Küllüoğlu[1], Çapan Konca[1], Fadiye Gökmen Uyanık[3], Gülnihan Üstündağ[4], Barış Güven[5], Dilek Yılmaz Çiftdoğan[4]

[1]University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of Pediatric Intensive Care, İzmir, Turkey
[2]İzmir Katip Çelebi University Faculty of Medicine, Department of Pediatric Intensive Care, İzmir, Turkey
[3]University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of Child Health and Diseases, İzmir, Turkey
[4]University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of Pediatric Infection, İzmir, Turkey
[5]University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of Pediatric Cardiology, İzmir, Turkey

Abstract

Fever and rash are a common symptom combination in children. Etiological studies are carried out primarily for the most common diseases. For this reason, in the period of the new Coronavirus disease-2019 (COVID-19) pandemic, especially COVID-19-related multi-inflammatory syndrome (MIS-C) comes to mind in children with this combination. Measles infection was detected in an 18-month-old Syrian girl who was hospitalized with the diagnosis of fever, conjunctivitis, pneumonia, maculopapular rash during the COVID-19 pandemic period. The case died with pneumonia and septic shock. With this case, we wanted to emphasize that during the COVID-19 pandemic, and measles should also be considered in the differential diagnosis of MIS-C in cases with fever, maculopapular rash and conjunctivitis.

Keywords: Measles, COVID-19, MIS-C, pediatric intensive care, pneumonia

Öz

Çocuklarda ateş ve döküntü sık görülen belirti kombinasyonudur. Etiyolojik araştırmalar öncelikle en yaygın görülen hastalıklara yönelik yapılmaktadır. Bu nedenle yeni Koronavirüs hastalığı-2019 (COVID-19) pandemisi döneminde bu kombinasyonu taşıyan çocuklarda özellikle COVID-19 ilişkili multi-enflamatuvar sendrom (MİS-C) akla gelmektedir. COVID-19 pandemi döneminde ateş, konjonktivit, pnömoni, makulopapüler döküntü ile yatan 18 aylık Suriyeli kız olguda, kızamık enfeksiyonu saptanmıştır. Olgu pnömoni ve septik şok kliniği ile kaybedilmiştir. Biz bu olgu ile COVID-19 pandemisi döneminde özellikle ateş, makülopapüler döküntü ve konjonktivitle gelen olgularda MİS-C ayırıcı tanısında kızamığın da düşünülmesi gerektiğini amaçladık.

Anahtar Kelimeler: Kızamık, COVID-19, MİS-C, çocuk yoğun bakım, pnömoni

Introduction

The "Novel Coronavirus disease-2019 (COVID-19)" spread rapidly all over the world, starting from the city of Wuhan, Hubei province of China, at the end of 2019 and caused many deaths.[1] The World Health Organization (WHO) declared COVID-19 as a pandemic on 11 March 2020.[2]

COVID-19 in children usually has a mild course. However, towards the end of April 2020, serious cases of COVID-19-related illness in previously healthy children began to be reported in many countries. Later, the Center for Disease Control and Prevention and WHO defined COVID-19-associated multi-inflammatory syndrome (MIS-C), presenting with fever, maculopapular rash, conjunctivitis and various organ involvements in children.[3]

It is stated that many infectious and inflammatory conditions such as Kawasaki disease, other viral infections, sepsis, and

Address for Correspondence/Yazışma Adresi: Doğa Lüleyap, University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of Pediatric Intensive Care, İzmir, Turkey
E-mail: doga071@windowslive.com **ORCID ID:** orcid.org/0000-0002-8201-0928
Received/Geliş Tarihi: 24.03.2021 **Accepted/Kabul Tarihi:** 23.04.2022

vasculitis should be considered in the differential diagnosis of MIS-C. The presence of many diseases in the differential diagnosis complicates the diagnosis of MIS-C.[4]

Measles is a highly contagious rash disease caused by an RNA virus of the paramyxoviridae family.[5]

In measles, a prodrome period manifested by cough, cold, conjunctivitis and fever are followed by the formation of typical maculopapular rashes.[6] Measles infection, which can cause serious complications, can result in death, especially due to panencephalitis and pneumonia.[7]

Our aim in this article is to present an 18-month-old Syrian patient, who presented with fever, pneumonia, conjunctivitis, and maculopapular rash and died due to septic shock, and to remind the necessity of considering measles infection in the differential diagnosis of MIS-C.

Case Report

An 18-month-old female patient was admitted to our hospital because of high fever, diarrhea and insufficient nutrition that had been going on for 3 days. She was weak and had cachectic appearance. Her body weight was 7 kg (<3 percentile), her height was 72 cm (<3 percentile), her body temperature was 39.5 °C, her heart rate was 140/min/rhythmic, her blood pressure was 85/50 mmHg, her respiration rate was 36/min, and SpO_2 was 98% (at room air). The patient had dry oral mucosa, cracked lips, sunken eyeballs, and a maculopapular rash (Figures 1, 2). On respiratory examination, there were prominent rales in the bilateral middle zone on auscultation, and diaper dermatitis was observed in the genital area.

Although the anamnesis reliability was low due to the fact that the family was from Syria, it was learned that the child was healthy before, there was no one in the family with similar symptoms, and they lived in a tent. There was no history of contact person in terms of COVID-19. The patient was considered as a possible COVID-19 case due to fever and respiratory distress, and droplet and contact isolation precautions were taken and she was hospitalized.

In the initial laboratory tests, the results were as follows: leukocyte: 13.000/mm^3, 57% neutrophil dominance, lymphocyte 38.9%, Hb: 10.4 gr/dL, Htc: 33%, platelet: 57.8000/mm^3, blood glucose: 83 mg/dL, urea: 48 mg/dL, creatinine: 0.6 mg/dL, Na: 131 mmol/L, K: 4.26 mmol/L, Ca: 9.4 mg/dL, aspartate transaminase (AST) 67 U/L, alanine transaminase (ALT) 27 U/L, C-reactive protein 88 mg/L (0.10-2.80), procalcitonin 37.1 ng/L (0.04-0.1), Pz: 14 sec, aPTZ: 47.7 sec, international normalized ratio (INR): 1.18, D-dimer 1.540 µg/mL (0-440) troponin was <2.5 ng/L (negative), BNP: 155.28 ng/L (2-100). Complete urinalysis was normal, electrocardiogram was consistent with sinus tachycardia. There was infiltration in the bilateral lower zones on the chest X-ray (Figure 3a). Thorax computed tomography (CT) revealed peripheral and centrally located multifocal consolidated areas in the bilateral lung parenchyma and ground glass densities around it. Thorax CT was reported by the radiology department as consistent with COVID-19 pneumonia (Figure 3b).

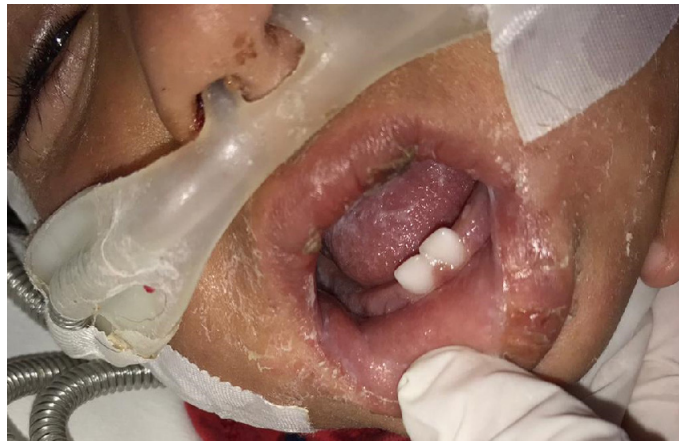

Figure 1. Koplik spot, dried and cracked lips

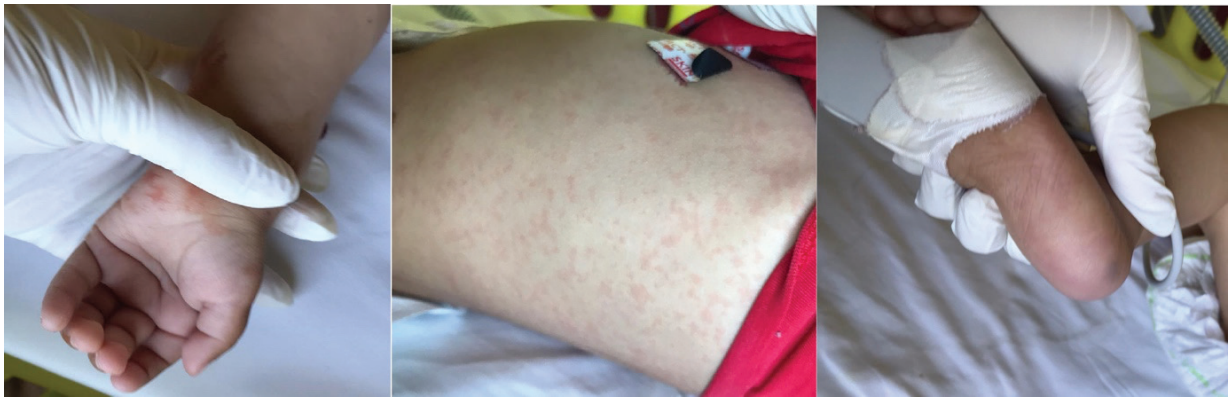

Figure 2. Exanthema appearance on the erythematous ground on the trunk

In the nasopharyngeal and oropharyngeal swab samples taken twice, COVID-19 polymerase chain reaction (PCR) was negative. High-flow nasal cannula (HFNC) oxygen therapy was initiated to the patient with respiratory distress. Considering pneumonia and possible COVID-19, oseltamivir, teicoplanin, cefotaxime and hydroxychloroquine treatments were started. The patient was hydrated. On the 3rd day of the follow-up, the patient developed increased respiratory distress and impaired consciousness; The child was intubated due to respiratory failure and was taken to the intensive care unit. Adrenaline infusion was started to the patient with fluid-resistant septic shock. In the examinations, leukocytes: 4.700/mm^3, lymphocytes: 3.000/mm^3, Hb: 7.5 gr/dL, Htc: 23%, platelets: 331.000/mm^3, blood glucose: 100 mg/dL, urea: 20 mg/dL, creatinine: 0.4 mg/dL, Na: 143 mmol/L, K: 4.1 mmol/L, Ca: 7.4 mg/dL , AST 86 U/L, ALT 21 U/L, C-reactive protein 18 mg/L (0.10-2.80), procalcitonin 16.9 ng/L (0.04-0.1), Pz: 13 sec, aPTZ: 43.6 sec, INR: 1.15, fibrinogen: 270 mg/dL, D-dimer: 2.380 µg/mL (0-440) troponin: <2.5 ng/L (negative), BNP: 200 ng/L (2-100). In the new chest radiograph, there was an increase in infiltration in the bilateral pericardiac area. On echocardiography, systolic functions were normal, jet flow in the mitral valve was 1st degree mitral insufficiency and there was no myocardial dysfunction.

In the differential diagnosis of the patient who was in the septic shock, toxic shock, Kawasaki disease, MIS-C, and viral eruptive diseases were considered. Immune globulin levels were within normal limits for age. CMV, HIV, hepatitis, EBV, and Parvovirus serologies were sent. Antibiotic therapy was changed to meropenem, vancomycin, and clindamycin. Intravenous immunoglobulin 2 g/kg and acetylsalicylic acid 5 mg/kg/day were started. The severe acute respiratory syndrome coronavirus-2 bronchoalveolar lavage PCR test for the patient who was followed up on mechanical ventilator was negative. Since she had fever, maculopapular rash, and pneumonia clinic and the vaccination status of the patient could not be known because she was from Syria, measles serology was sent. There was no growth in the blood, urine and bronchoalveolar lavage cultures of the patient. The patient died in the 12th hour of the intensive care monitorization. COVID-19 immunoglobulin M and G were found to be negative, measles IgM >200 U/L (>25) was high titer positive as postmortem. No pathology was detected in other viral serology tests. Based on the current findings, it was thought that the patient died due to complications of measles infection (pneumonia, septic shock).

Discussion

Fever, rash, conjunctivitis, pneumonia and shock seen in our patient made us think of the diagnosis of MIS-C in the current period. Because the patient was Syrian and her vaccination status was unknown, measles was suspected, but the diagnosis was made postmortem. Our patient died due to pneumonia and septic shock. This case is presented to emphasize that measles should not be forgotten among the rash diseases that can be confused with MIS-C.

In MIS-C cases, findings related to many systems are seen together with fever. These findings are not specific and the differential diagnosis includes non-infectious etiologies such as Kawasaki disease, severe acute COVID-19 infection, bacterial sepsis, toxic shock syndrome, other viral infectious diseases as well as oncological or inflammatory conditions.[8,9] Measles infection is one of the infectious viral rash diseases that should be considered in the differential diagnosis of MIS-C. Fever, cough, non-purulent conjunctivitis, diarrhea, and maculopapular rashes seen in measles infection are the most common findings in MIS-C. In the skin findings of MIS-C, papulovesicular, varicella-like rash and urticarial lesions can also be seen apart from a maculopapular rash. While koplik spot is seen specifically in oral mucosal involvement of measles infection, non-specific oral mucosal changes and dry red lips

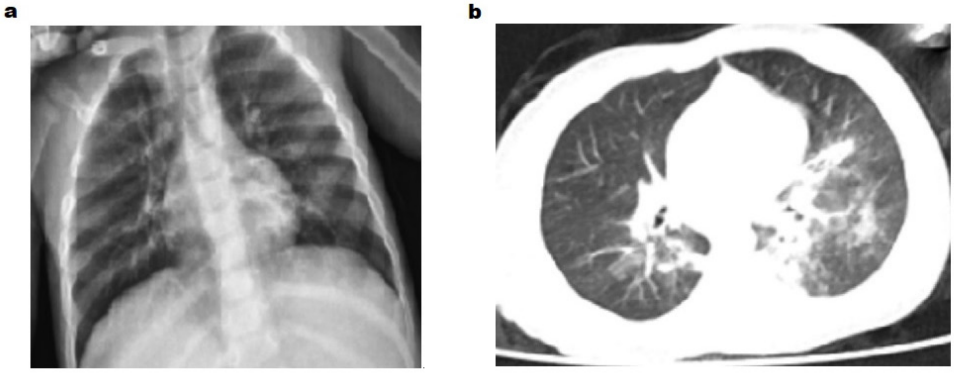

Figure 3. a. Pneumonic infiltration in bilateral lower zone in a posterior anterior chest X-ray, **b.** Consolidated area in bilateral lung parenchyma and ground-glass density image around it in thorax CT

CT: Computed tomography

Table 1. Comparison of the case in terms of MIS-C and measles

	Case	MIS-C	Measles
Findings	Fever, cough, diarrhoea, conjunctivitis, respiratory distress, rash, pneumonia, shock	Fever Two or more system involvement (rash, conjunctivitis, shock, abdominal pain, diarrhea, cough, dyspnea, cardiac dysfunction, renal-neurological-hematological findings)	Fever, malaise, cough, flu, conjunctivitis, diarrhea, pneumonia and maculopapular rash
Laboratory	Leukopenia, anemia high CRP and procalcitonin, hypoalbuminemia Measles, IgM positivity	High lymphopenia, neutrophilia, anemia, thrombocytopenia, CRP, D-dimer, procalcitonin, ferritin, fibrinogen, Hypoalbuminemia, high liver enzymes, High troponin and BNP, history of COVID-19 infection or contact (positive serology, antigen or PCR test)	Thrombocytopenia, leukopenia measles, IgM positivity
Radiology	Ground-glass appearance around the consolidated area in the lung parenchyma (interstitial pneumonia)	Diffuse consolidation, pleural effusion, ground glass opacities	Diffuse consolidated area in lung parenchyma consistent with interstitial pneumonia

MIS-C: Multi-inflammatory syndrome, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction, CRP: C-reactive protein, Ig: Immunoglobulin

are present in MIS-C. In addition, hand and foot edema, which is not seen in measles, can develop in MIS-C.[10] There are also similarities in laboratory and chest radiography findings of MIS-C and measles infection. Table 1 shows the comparison of our case in terms of MIS-C and measles findings. In the light of these findings, MIS-C was first considered in our patient due to the COVID-19 pandemic period, and measles infection was also investigated in the differential diagnosis.

The diagnosis of measles is made clinically. However, it is necessary to apply to the laboratory in different clinical courses. Serology (measles IgM positivity) is the most common laboratory method for diagnosing measles infection.[7] Due to the similarity of our case with MIS-C, the diagnosis could only be made postmortem with measles IgM positivity.

There is no specific antiviral drug against measles and its complications, but ribavirin treatment may be preferred for patients younger than 12 months, who have pneumonia due to measles and require respiratory support.[11] WHO recommends that all children with acute measles infection be given vitamin A.[12] Vitamin A acts as a kind of immune modulator and increases the antibody response.[13] Our patient died due to pneumonia and septic shock at the 12th hour of her intensive care hospitalization, and vitamin A treatment could not be given since the diagnosis was made postmortem.

Vaccination is the most effective way to prevent measles. The measles vaccine has been in the vaccine program since the 1970s. Since 2006, measles- mumps- rubella triple vaccine has been administered as a total of 2 doses in the 12th month and the first grade of primary education. As of July 1, 2020, it has been administered as an additional dose in the 9th-11th months in epidemic regions[14] WHO recommends that all routine vaccines be administered as planned during the COVID-19 outbreak. Our patient was thought to be unvaccinated because she was Syrian and lived in poor socioeconomic conditions.

Conclusion

Apart from MIS-C, measles infection should be considered in children presenting with fever, conjunctivitis, rash and respiratory symptoms during the COVID-19 pandemic period.

Ethics

Informed Consent: Written informed consent was obtained from the parents for the publication of their personal and clinical details with any identifying images in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: D.L., A.B.A., Design: D.L, A.B.A., P.K., Ç.K., Data Collection or Processing: D.L., A.B.A., F.G.U., Analysis or Interpretation: A.B.A., B.G., D.Y.Ç., G.Ü., Literature Search: D.L., A.B.A., Writing: D.L., A.B.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020.
2. WHO characterizes COVID-19 as a pandemic. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen Accessed Apr 14, 2020.
3. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. 2020;395:1607-8.

4. Shulman ST. Pediatric Coronavirus Disease-2019-Associated Multisystem Inflammatory Syndrome. J Pediatric Infect Dis Soc. 2020;9:285-6.
5. Moss WJ. Measles. Lancet. 2017;390:2490-502.
6. Perry RT, Halsey NA. The clinical significance of measles: a review. J Infect Dis. 2004;189(Suppl 1):S4-16.
7. Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book), 12th ed, Atkinson W, Wolfe C, Hamborsky J (Eds), The Public Health Foundation, Washington, DC 2011.
8. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, et al. Multisystem inflammatory syndrome in US children and adolescents. N Engl J Med. 2020;383:334-46.
9. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, et al. Multisystem inflammatory syndrome in children in New York State. N Engl J Med. 2020;383:347-58.
10. Naka F, Melnick L, Gorelik M, Morel KD. A dermatologic perspective on multisystem inflammatory syndrome in children. Clin Dermatol. 2021;39:163-8.
11. Pal G. Effects of ribavirin on measles. J Indian Med Assoc. 2011;109:666-7.
12. Huiming Y, Chaomin W, Meng M. Vitamin A for treating measles in children. Cochrane Database Syst Rev. 2005;2005:CD001479.
13. World Health Organization. Measles vaccines: WHO position paper. Measles and Vitamin A. Available from: http://www.who.int/wer/2009/wer8435.pdf#page=3 (Accessed on July 08, 2015).
14. T.C. Sağlık Bakanlığı Çocukluk Dönemi Aşı Takvimi, 2020. Erişim adresi: https://asi.saglik.gov.tr/asi-takvimi2. Erişim tarihi: 07.11.2021