

Case Report

A new mimicker of the multisystem inflammatory syndrome in children: Influenza

Çocuklarda multisistem inflamatuvar sendromunun yeni bir taklitçisi: Influenza

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ABSTRACT

Multisystem inflammatory syndrome in children (MIS-C) might present a severe clinical course that clinicians should promptly treat. However, distinguishing other illnesses similar to MIS-C could be confusing. Here, we presented a two-year-old boy diagnosed with MIS-C owing to three days of fever, gastrointestinal findings, mucosal involvement, and elevated inflammatory markers, whose respiratory virus panel resulted in influenza A.

Keywords: children, influenza, multisystem inflammatory syndrome in children

ÖZET

Çocuklarda multisistem inflamatuvar sendrom (MIS-C), klinisyenlerin hızlı bir şekilde tedavi etmesini gerektiren ciddi bir klinik seyir gösterebilir. Ancak MIS-C'ye benzer diğer hastalıkları ayırt etmek de kafa karıştırıcı olabilir. Burada, üç günlük ateş yüksekliği öyküsü, gastrointestinal bulguları, mukozal tutulumu ve yüksek inflamatuvar belirteçleri olması nedeniyle MIS-C tanısı alan ve sonrasında solunum virüs paneli influenza A ile sonuçlanan iki yaşında bir erkek çocuğu sunduk.

Keywords: çocuk, influenza, multisistem inflamatuvar sendrom

INTRODUCTION

Concerns about differential diagnosis between coronavirus invasive diseases 2019 (COVID-19) and other respiratory viral infections existed during the first winter of COVID-19 in 2020. This concern was unfounded because we did not observe many respiratory viruses other than SARS-CoV-2. However, since the advent of the multisystem inflammatory syndrome in children (MIS-C), the same problem has developed due to confusion regarding the manifestations of many diseases, including Kawasaki disease, septic shock syndrome,

bacterial infections, and rheumatologic diseases. The diagnostic criteria for MIS-C could readily be met by other illnesses defined by hyperinflammatory events resulting in a protracted fever. This case report is an example of this hesitation in our clinical experience.

CASE REPORT

A two-year-old boy was admitted to the children's emergency department due to three days of fever,

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nonproductive cough, four times vomiting, headache, and stomachache. On his physical examination, auscultation of the heart and lungs was normal, the tonsils seemed hyperemic but in regular size, and the tympanic membrane was normal, whereas the abdomen was tender with no organomegaly. Meningeal irritation signs were negative. There was conjunctival hyperemia, white tongue, macular, blanching, trunk rash on the skin, and mucosal inspection (Figure 1). In addition, left cervical lymphadenopathy was noted.



Figure 1. Skin and mucosal presentation of the patient, including nonpurulent conjunctivitis (A), white-coated tongue (B), and rash (C).

Based on the mother's declaration, the patient's severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) polymerase chain reaction (PCR) was positive six weeks ago. Apart from this, background and family history were unremarkable.

On the laboratory analyses, white blood cell (WBC) was $7.4 \times 10^3/\mu\text{L}$, absolute neutrophil count (ANC) was $6.4 \times 10^3/\mu\text{L}$, absolute lymphocyte count (ALC) was $0.4 \times 10^3/\mu\text{L}$; hemoglobin was 12.2 gr/dL, platelets (PLT) were $187 \times 10^3/\mu\text{L}$, procalcitonin (PCT) was 0.99 $\mu\text{g/L}$, C-reactive protein (CRP) was 11.8 mg/L, albumin was 4.3 g/dL, blood sodium was 133 mmol/L, D-dimer was 620 $\mu\text{g/L}$ FEU, fibrinogen was 269.15 mg/dL, troponin I was 15.38 ng/L, ferritin was 59 $\mu\text{g/L}$, triglyceride was 52

mg/dL. The day after, CRP, PCT, and D-dimer increased to 53.5 mg/L, 1.36 $\mu\text{g/L}$, and 2930 $\mu\text{g/L}$ FEU, respectively. A blood culture, urine culture, and a respiratory virus panel were obtained. PCR for SARS-CoV-2 was negative. SARS-CoV-2 immunoglobulin (Ig) M was negative at 0.38; IgG was positive at 2.35.

Accordingly, the patient was admitted to the pediatric infectious diseases ward. Differential diagnoses included MIS-C, Kawasaki disease, and bacteremia. Ceftriaxone at 100 mg/kg/day and intravenous immunoglobulin (IVIG) at 2 mg/kg for 12 hours infusion were started. On the echocardiogram, no aneurism or myocardial dysfunction was seen. The patient's vital signs and blood pressure were normal during the hospitalization. The steroid was not initiated until clarifying the diagnosis. Two days after the patient was admitted to the ward, the respiratory virus panel resulted in Influenza A. Oseltamivir was initiated as soon as the PCR had resulted. Afterward, the patient's fever went down.

DISCUSSION

MIS-C was first introduced in the United Kingdom as a hyperinflammatory shock associated with COVID-19, similar to Kawasaki disease in a cluster of eight children (1). As similar cases were reported globally, diagnostic criteria were arranged by the Centers for Diseases Control and Prevention and the World Health Organization (2,3). These criteria briefly include an unrelenting fever, elevation of anti-inflammatory markers, at least two organ-system involvement, no alternative diagnoses, and evidence of SARS-CoV-2 infection.

In our patient, three days of an unintermittent fever, elevated CRP and PCT, lymphopenia, gastrointestinal findings, lymphadenopathy, and mucosal involvement, including the white tongue, nonpurulent conjunctivitis, and rash, abnormal coagulation parameter, as well as epidemiologic link were noted compatible with MIS-C. Hence, IVIG was administered to the patient to prevent a sudden clinical worsening due to cardiac dysfunction. The reason for being reluctant to initiate the steroid treatment was his mild mucosal involvement, which was not as distinct as in patients with MIS-C. Kawasaki disease could also not be excluded since the patient would have fulfilled its diagnostic criteria if the fever had continued for two more days. Yeo et al. came out with a hypothesis for distinguishing between typical Kawasaki disease and MIS-C that stressed the importance of PLT. Kawasaki disease is presented more likely with thrombocytosis, whereas MIS-C with thrombocytopenia (4). In this context, our patient's PLT was

not favorable, being at the normal range. However, lymphopenia was seen, referenced as the MIS-C component.

Recently, reports of mistaken MIS-C cases have been increasing. Dworsky et al. presented a case series with prolonged fever and gastrointestinal symptoms that first suggested MIS-C; later, the patients were diagnosed with bacterial enteritis (5). Similarly, Kara et al. presented two cases considered MIS-C until gram-negative bacteria were grown in their blood cultures (6).

Detecting influenza A in the respiratory virus panel was not surprising in the seasonal term. However, it was confusing for the clinical presentation of the patient. Influenza A causes sudden fever, headache, myalgia, and malaise, as well as respiratory tract symptoms, such as cough, sore throat, and rhinitis (7). Younger children may present gastrointestinal symptoms, such as diarrhea, nausea, vomiting, and poor appetite, all of which can also be seen in MIS-C (8). Although influenza may cause prolonged fever, as in MIS-C, a rash is rarely reported (9). As for the white tongue, no co-occurrence with influenza was encountered in the literature except for several case reports that presented Kawasaki disease and influenza infection together (10,11).

One of the most prominent findings in laboratory analyses of MIS-C is lymphopenia (12). On the other hand, influenza A may present with leukopenia in the early infection course (13). Our patient's acute phase reactants, including CRP and procalcitonin, were relatively low compared to those observed during the MIS-C course. In a multicenter study in which 614 MIS-C patients were evaluated, more than half of the patients had CRP greater than 100 mg/L, which supports that MIS-C exhibits significant elevation of inflammatory markers (12).

In our case, despite influenza A being detected in the respiratory virus panel, the patient's COVID-19 serology was positive, and all the other clinical and laboratory analyses were in line with MIS-C. Therefore, MIS-C could not be excluded. On the other hand, an over-diagnosing attitude increases when "MIS-C-like" patients arrive in clinical practices. We thought at this stage that the vague skin and mucosal involvement could be due to both the feverish condition and MIS-C.

Although the MIS-C criteria may be met for other inflammatory diseases, the Centers for Disease Control and Prevention (CDC) criteria of "no alternative plausible diagnoses" and "severe illness requiring hospitalization" may support excluding patients with other di-

agnoses in circumstances of confusion. In fact, the CDC only recently released updated diagnostic criteria for MIS-C in January 2023, which may lead to a reduction in the number of cases of MIS-C that are incorrectly identified (2).

Consequently, MIS-C is a disease that necessitates immediate treatment due to its abrupt onset of cardiac problems. However, with the fear of MIS-C, other alternative and most widely seen illnesses should not be omitted to explore. A respiratory virus panel should be obtained in seasons where seasonal viral infections are prevalent, especially in prolonged fever.

Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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