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Case Report

Neurological Complications in MIS-C: Case Report

MIS-C'De Nörolojik Komplikasyonlar: Vaka Sunumu

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ABSTRACT

COVID-19 has seriously affected children and the whole world. Pediatric multi-system inflammatory syndrome (MIS-C), a new syndrome that has not been known before, has been described. Although MIS-C may progress with different clinical manifestations in children, neurological involvement is reported relatively rarely. A 12-year-old girl with cerebral palsy and motor mental retardation was admitted to the emergency department with complaints of cough, fever, mouth sores and malnutrition. As a result of the evaluation, the patient was hospitalized to investigate the etiology of the fever and empirical antibiotic treatment was started, and she developed a rash on the 3rd day and tonic-clonic convulsions on the 5th day. The patient was hospitalized in the pediatric intensive care unit (PICU), and COVID-19 IgG and IgM were positive. Cerebral imaging of the patient was reported as normal. The patient with fever, rash, convulsions lasting longer than five days, and compatible laboratory results were diagnosed with MIS-C. Intravenous immunoglobulin (IVIG) and methylprednisolone treatments were started, and the patient was discharged on the 14th day of hospitalization, whose condition improved. This case is presented as an example of the rare neurological involvement of MIS-C. Detailed clinical investigation and neurological examination are required to exclude neurological sequelae of COVID-19 during the pandemic. The development of general guidelines that can combine them would be instructive.

Keywords: *mis-c, COVID-19, neurological, complication*

ÖZET

COVID-19 tüm dünyayı etkilediği gibi çocukları da ciddi şekilde etkilemiştir. Daha önce tanımlanmamış yeni bir sendrom olan pediatrik multi-sistem inflamatuar sendrom (MIS-C) tanımlanmıştır. MIS-C çocuklarda değişik klinik tutulumlarla seyredebilse de nörolojik tutulumları görece nadir bildirilmektedir. Serebral palsi ve motor mental retardasyonu olan 12 yaşında kız hasta acil servise öksürük, ateş, ağızda yaralar ve malnütrisyon şikayetleri ile başvurmuştur. Yapılan değerlendirme sonucunda ateş etyolojisinin araştırılması için servise yatırılan ve ampirik antibiyotik tedavisi başlanan hastada üçüncü günde döküntü, beşinci günde ise tonik-klonik konvülziyon gelişmiştir. Hasta çocuk yoğun bakım ünitesine (ÇYBÜ) yatırılmış ve tetkiklerinde COVID-19 IgG ve IgM pozitif gelmiştir. Hastanın serebral görüntülemeleri normal olarak raporlanmıştır. Beş günden uzun süren ateş, döküntü, konvülziyon ve uyumlu laboratuar sonuçları olan hastaya MIS-C tanısı konmuştur. Hastaya intravenöz immunglobulin (IVIG) ve metilprednizolon tedavileri başlanmış, durumu düzelen hasta yatışın 14. gününde taburcu edilmiştir. Bu vaka, MIS-C'nin nadir görülen nörolojik tutulumuna bir örnek olduğundan sunulmuştur. Pandemi süre–

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cinde COVID-19'un nörolojik sekellerini dışlamak için ayrıntılı klinik araştırma ve nörolojik muayene gereklidir. Bunları birleştirebilecek genel kılavuzların geliştirilmesi yol gösterici olacaktır.

Keywords: *mis-c, COVID-19, nörolojik, komplikasyon*

INTRODUCTION

The novel coronavirus disease 2019 (COVID-19) has affected thousands of children worldwide. Although it usually has a mild course in children, uncertain clinical pictures ranging from asymptomatic to severe respiratory distress can be seen in COVID-19. Finally, pediatric multisystem inflammatory syndrome (MIS-C) has been defined as a new clinical entity (1). MIS-C presents various organ involvements, but neurological manifestations are not commonly reported in children. In this report, we aimed to report a case of MIS-C admitted with seizures.

CASE REPORT

A 12-year-old girl, who was followed up with the diagnosis of cerebral palsy and mental motor retardation, was admitted to the emergency service with complaints of fever, cough, mouth sores and malnutrition for a week. It was learned from the patient's history that the diagnosis of cerebral palsy existed for a long time, and that she had motor-mental retardation related to it, but that she did not have an additional disease and especially a history of seizures/convulsions.

In the first physical examination, the child had a pale appearance. Her vital signs were as follows: body temperature: 38,5°C, oxygen saturation (in air room): 100%, respiratory rate: 40/minute, heart rate: 145/minute, manually measured blood pressure: 110/65 mmHg. The patient was awake, general condition was poor, eyeballs were sunken, oral mucosa was dry-red, and lips were chapped. Other system examinations were normal.

The laboratory values of the patient at the first hospital admission were as follows: White blood cell: 18.10x10^9/L, hemoglobin: 16.0 g/dL, platelet: 272.000/uL, neutrophil ratio: 85.4%, lymphocyte ratio: 12%, C-Reactive Protein: 3.0 mg/L, Alanine Transferase (ALT): 5.3 U/L, Aspartate Transferase (AST): 23.4 U/L, Sodium: 141 mmol/L, Potassium: 4.5 mmol/L, Calcium: 9.66 mg/dL, and Magnesium:1.56 mg/dL. The patient was admitted to the ward to support nutrition and to investigate the etiology of the fever.

Empirical antibiotic (ceftriaxone 50mg/kg/day) treatment was started for the patient, who was followed up in the general pediatrics clinic. The patient had a maculopapular rash on the 3rd, and generalized tonic-clonic seizures were added to the clinical picture on the 5th day. There was no known history of seizures, and the fingertip blood sugar measured during the seizure was not hypoglycemic, and there was no electrolyte imbalance that would cause seizures. The patient was transferred to the pediatric intensive care unit (PICU) on the 5th day of the follow-up due to this developing seizure. Antibiotic therapy was revised (vancomycin, meropenem) due to persistent fever. COVID-19 Immunoglobulin G and Immunoglobulin M antibodies of the patient who did not have any culture growth were positive. There was no abnormality in chest X-ray and cranial brain tomography (CT) imaging. Diffusion restriction in favor of edema in the cortical and juxtacortical areas was detected in the left frontal and left occipital lobes on diffusion magnetic resonance imaging (Figure 1).

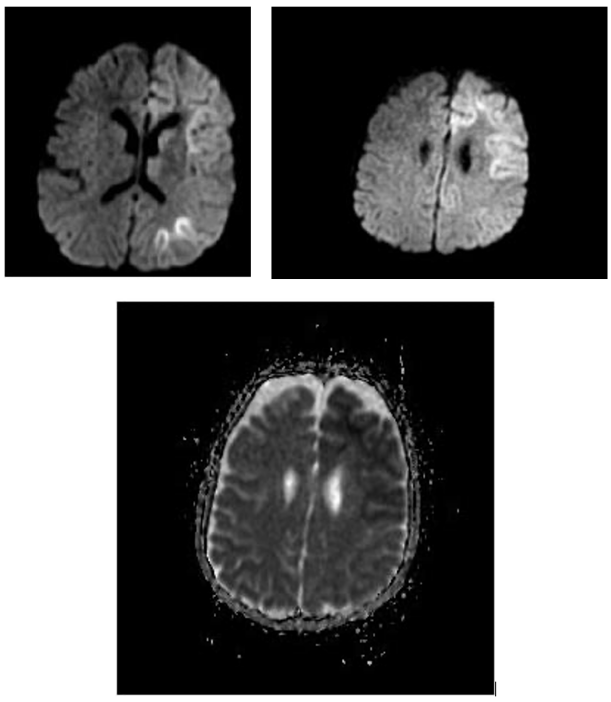

Figure 1. Diffusion restriction in favor of edema in the cortical and juxtacortical areas in the left frontal and left occipital lobes in diffusion magnetic resonance imaging.

The cervical MR angiography of the patient was reported as normal. Abdominal ultrasonography exami–

nation was also reported as normal. No pathology was detected in the cardiac electrocardiography examination. The patient with fever, rash, increase in inflammation markers and seizures lasting longer than five days, and a positive COVID-19 antibody diagnosis, was diagnosed with MIS-C (Table 1) and intravenous immunoglobulin (IVIG) (0.5mg/kg/day) (5 days) and methylprednisolone (2 mg/kg/day) treatments were started.

Table 1. Case definition of MIS-C as per CDC

An individual aged <21 years, presenting with fever (>24 hours): **12 aged and fever lasting five days**
Laboratory evidence of inflammation CRP ↑ ESR ↑ Fibrinogen ↑ Procalcitonin ↑ D-dimer ↑ Ferritin ↑ LDH ↑ IL-6 ↑ Neutrophilia Lymphocytopenia Hypoalbuminemia
Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the four weeks before the onset of symptoms: SARS-COV-2 PCR positives
No plausible alternative diagnoses
Multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological): Respiratory, dermatologic and neurological involvement

The seizure did not recur under levetiracetam treatment. On the 4th day of intensive care follow-up, his condition remained stable, and he was transferred to the pediatrics service. He was discharged on the 14th day of his hospitalization, and the child was taken under neurology follow-up. The patient's consent was obtained for this case study.

DISCUSSION

In December 2019, cases of severe pneumonia of unknown cause began to be seen in Wuhan, the capital of China's Hubei province. On January 7, 2020, the agent was identified as a novel coronavirus that has not been previously detected to cause disease in humans (2019-n COV). Later, the name of the 2019-nCOV disease was accepted as COVID-19, and the causative agent was named SARS-COV-2 due to the close resemblance of its agent to SARS-COV (2, 3). As of November 12, 2022, the COVID-19 pandemic has affected 222 countries worldwide, with 640 million positive cases and 6.6 million deaths (4). At first, a mild clinical picture was noted in children. However, in the continuation of the pandemic, a picture associated with COVID-19, showing clinical features similar to Kawasaki disease, with multisystemic inflammation, emerged epidemiologically and was named MIS-C (5). Fever, mucocutaneous findings (rash, conjunctivitis, hand/foot edema, red/chapped lips, and strawberry tongue), myocardial dysfunction, cardiac conduction abnormalities, shock, gastrointestinal symptoms, respiratory findings, and lymphadenopathy are among the main symptoms of MIS-C (1).

Regarding the neurological involvement in COVID-19, severe neurological manifestations (encephalopathy, meningoencephalitis, stroke, seizure, Guillain-Barré syndrome, acute disseminated encephalomyelitis) were mainly identified in adults (6), while a small number of reported cases in children is noteworthy. In a study of adult patients with COVID-19 and neurological symptoms, 31% of patients reported ischemic infarction, 6% intracranial hemorrhage, and a small percentage reported nonspecific T2/fluid-attenuated inversion healing hyperintensity with diffusion restriction (7). The mechanism of neurological involvement in children with MIS-C remains unclear, but it is generally thought to be a different mechanism from the associated cerebrovascular infarction in adults. Mechanisms have been proposed to explain how SARS-CoV-2 might induce neurological damage: the most notable mechanism was a direct viral infection of the nervous system via ACE 2 receptors and inflammatory damage mediated by cytokine release (8). In addition, some opinions consider it may be related to acute necrotizing encephalopathy, a para-infection mainly defined in the pediatric population (9). Also, another entity called reversible splenial lesion syndrome (RESLES) is discussed. It is characterized by a transient lesion of the splenium of the corpus callosum associated with encephalitis, se-

halitis/encephalopathy and reversible spleen lesion has been defined a separate syndrome associated with various viral infections (10).

In our case, there were complaints of fever and cough on admission. The patient was followed up to support the decreased oral intake due to stomatitis. On the 3rd day of the follow-up, a maculopapular rash developed. Then, on the 5th day, she had a generalized tonic-clonic seizure. During the seizure, the patient's temperature was low and not in an increasing trend. More severe seizure etiologies, such as hypoglycemia, electrolyte imbalance, intracranial infection, mass, and bleeding were excluded. In our patient, lumbar puncture (LP) was not performed for the etiology of seizures since there were signs in favor of edema in the diffusion MR imaging. Pathologies that may cause this situation in the central nervous system were excluded by imaging methods. The patient had no known COVID-19 contact and no previous infection information, but based on the number of cases in the country, we can assume that he got the disease due to the recent increase.

This case is an example of the neurological involvement of MIS-C. General guidelines combining detailed clinical investigations with the neurological examination are needed, particularly in pediatric patients from endemic areas, to exclude any severe neurological sequelae of COVID-19 during the pandemic.

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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