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Case Report

Multisystem Inflammatory Syndrome (MISC) in Adolescent with Recent COVID-19 Infection. Case Report Study

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Abstract

MIS-C syndrome has many similarities with Kawasaki Disease and Macrophage Activation Syndrome due to patients revealed significant improvement with immunomodulatory drugs. A 15-year-old male came to the emergency department with 6 days fever and diarrhea. Medical history reports SARS - COVID19 infection 5 weeks ago. Due to the increased inflammatory markers such as CRP and procalcitonin as well as troponin, ferritin, d-dimer and LDH in combination with diarrhea and rash diagnosis of MISC was made. Treatment was started with IVIG for 2 days and aspirin for 5 days. The patient remained for the completion of the treatment and came out without symptoms. Instructed to continue treatment with peros aspirin 300 mg for 1 month. Reassessment was performed at the end of the treatment without pathological findings. Children with COVID-19 have been reported to have more frequent mild clinical symptoms than adults. Most children with COVID-19 having mild to moderate symptoms leading in most cases to well prognosis and improvement of symptoms in one week but in few cases may reveal multisystemic inflammatory reaction (MIS-C) which depends acute diagnosis and appropriate treatment.

Keywords: *COVID Disease; Inflammation; Multisystemic Inflammatory Reaction (MIS-C)*

Abbreviations

MIS-C: Multisystemic Inflammatory Reaction; CRP: C-Reactive Protein; IVIG: Immunoglobin g (IVIG)

Introduction

During first months of the COVID-19 pandemic some children developed serious but rare complication of a multisystemic inflammatory reaction (MIS-C) showed a temporal correlation between infection and onset of symptoms [1,2].

According to published studies, MIS-C after 2 to 6 weeks of SARS-CoV-2 infection in may develop high fever and non-specific symptoms including abdominal pain, vomiting, headache and fatigue in several cases conjunctival hyperemia and rash resembling Kawasaki disease [3-5].

In more severe cases multiorgan failure and cardiogenic shock may occur. Laboratory tests revealed severe inflammation with elevated C-reactive protein (CRP), ferritin, troponin and type B natriuretic peptide and decreased levels of hemoglobin, platelets, and lymphocytes.

MIS-C syndrome has many similarities with Kawasaki Disease and Macrophage Activation Syndrome due to patients revealed significant improvement with immunomodulatory drugs [6]. As Kawasaki Disease on MIS-C may revealed cardiac symptoms such as coronary artery aneurysm. Immunoglobin g (IVIG) is the main and proven treatment for Kawasaki while some children with MIS-C may recover with support treatment [7].

Observation

A 15-year-old male came to the emergency department with 6 days fever and diarrhea. Started antibiotic treatment 2 days ago with amoxicillin/clavulanate without improvement of symptoms. Medical history reports SARS - COVID19 infection 5 weeks ago. Objective examination of the lungs and heart did not reveal any pathological findings but showed intense intestinal sounds with diffuse abdominal tenderness and diffuse urticaria-type rash on the abdomen and hands.

Laboratory examinations were found WBC: 14590/μl (W: 82.8%, L: 12.2%, M: 5.0%), Hgb: 34.4 mg/dl Ht: 11.7% PLT: 3470000/μl, CRP: 422.03 mg/dl, SGOT: 28U/L, SGPT: 29 U/L, LDH 402 U/L, TB 7.7 gr/dl, albumin: 3.8 gr/dl, Na 136 mmol/L, K 4,2 mmol/L, Ferr: 512 ng/ml, Procalcitonin - PC 1.55 ng/ml, APTT 41.8 sec, Fibrinogen 642 mg/dl, D-Dimers 1.67 μgr/ml, INR: 1.09 TKE 88 mm, hsTnI 19.5 pg/ml, IgG SARS - COV-2: 3500 U/ml, IgM SARS - COV-2: 0.35 U/ml.

Due to the increased inflammatory markers such as CRP and procalcitonin as well as troponin, ferritin, d-dimer and LDH in combination with diarrhea and rash diagnosis of MISC was made. Treatment was started with IVIG for 2 days: aspirin for 5 days and iv cefotaxime for 10 days.

Laboratory test repeated after 3 days WBC: 7290/μl (W: 42.1%, L: 45.9%, M: 5.0%), Hgb: 30.5 mg/dl Ht: 10.3% PLT: 4620000/μl, CRP: 163.9 mg/dl, SGOT: 31U/L, SGPT: 17 U/L, TB 7.9 gr/dl, albumin: 2.6gr/dl, Na 137 mmol/L, Ferr: 392 ng/ml, Procalcitonin - PC 0.85 ng/ml, APTT 35.8 sec, Fibrinogen 442 mg/dl, D-Dimers 1.77 μgr/ml, INR: 1.06 TKE 91 mm, hsTnI 5.1 pg/ml.

On the 3rd day of hospitalization, the fever stopped and reveled improvement of clinical sings. Abdominal and heart ultrasounds performed the first and third day showed no pathological findings.

On the 7th day of hospitalization, repeated laboratory tests were performed: WBC: 8690/μl (W: 55.4%, L: 31.9%, M: 9.0%), Hgb: 36.5 mg/dl Ht: 12.3% PLT: 4430000/μl, CRP: 9.7 mg/dl, SGOT: 57U/L, SGPT: 42 U/L, TB 9.1 gr/dl, albumin: 3.9 gr/dl, LDH 206 U/L, Na 139 mmol/L, Ferr: 115 ng/ml, Procalcitonin - PC 0.35 ng/ml, APTT 30.8 sec, Fibrinogen 322 mg/dl, D-Dimers 0.29 μgr/ml, INR: 1.02 TKE 52 mm, hsTnI < 5.1 pg/ml.

The patient remained hospitalized for completion of the treatment and came out without symptoms. Instructed to continue treatment with peros aspirin 300 mg for 1 month. Reassessment was performed at the end of the treatment without pathological findings.

Discussion

Children with COVID-19 have been reported to have more frequent mild clinical symptoms than adults [8]. Most children with COVID-19 having mild to moderate symptoms leading in most cases to well prognosis and improvement of symptoms in one week [9]. Most children with COVID-19 symptoms have mild symptoms however patients with moderate, severe, or critical symptoms such as pneumonia, hypoxia or acute respiratory distress syndrome have been described [10].

In a cohort study, 73% of pediatric patients had symptoms of fever, cough or dyspnea compared with 93% of adults while children revealed much lower rates of hospitalization 8.7%, while 1% to 1, 5% was admitted to ICU.

Some pediatric patients may have radiographic findings compatible with pituitary opacities suggestive of pneumonia. These findings may also occur in asymptomatic children or children with mild symptoms [11]. In addition, Qiu H., *et al*. reported that the prevalence of pneumonia with COVID-19 (53%) was higher than H1N1 influenza (11%).

Laboratory findings include lymphopenia (31%), leukopenia (19%) and elevated creatine-MB kinase and procalcitonin (17%). According to Xia W., *et al*. may appeared lymphopenia (35%), elevated ALT (25%), elevated creatine kinase (75%), CRP (45%) and procalcitonin (80%) [11].

In addition, prothrombin time and D-dimer levels were higher in patients needed ICU hospitalization. Zhou., *et al*. reported that elevated D-dimer levels were the major risk factor for severe disease and death in COVID-19 patients. Also elevated D-dimer levels were more common in infants than in other ages suggested infants may become more severe than older children after COVID-19 infection.

Similarly, in our work case study we identified similar laboratory findings such as lymphopenia and elevated levels of CRP, LDH, ferritin.

Although children with COVID-19 generally have less severe or even symptoms or are asymptomatic than adults, some children develop a significant systemic inflammatory response and have symptoms resembling severe form of Kawasaki disease [12].

Due to recent onset of the syndrome and its resemblance to Kawasaki disease, the regimens used for MISC are similar of guidelines of Kawasaki disease patients. The American College of Rheumatology (ACR) recently published guidelines for the treatment of MIS-C [12].

The ACR has recommended the use of intravenous immunoglobulin (IVIg) and/or high-dose corticosteroids as first-line treatment in these patients. Approximately 30 - 80% of patients do not respond to IVIg as monotherapy and may need complementary immunomodulatory treatment to control inflammation [13,14].

MISC from Kawasaki disease differentiates in resistance to IVIG therapy has been observed in less than 15% of patients [60]. Methylprednisolone (10 - 30 mg/kg/day for 3 - 7 days followed by a gradual reduction of oral prednisolone) and aspirin in some cases of severe patients may receive such as a second dose of IVIG, anakinra or infliximab [15,16].

Conclusion

Children with COVID-19 have been reported to have more frequent mild clinical symptoms than adults. Most children with COVID-19 having mild to moderate symptoms leading in most cases to well prognosis and improvement of symptoms in one week. Few cases may reveal multisystemic inflammatory reaction (MIS-C) which depends acute diagnosis and appropriate treatment.

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