

## SEVERE POST-COVID-19 MULTISYSTEM INFLAMMATORY SYNDROME IN 15-YEAR-OLD GIRL: A CASE REPORT

Vanja Trajkovska<sup>1,3</sup>, Biljana Andonovska<sup>1,3</sup>, Maja Mojsova Mijovska<sup>1,4</sup>, Amela Muminovic<sup>1</sup>, Saso Popovski<sup>1</sup>, Gjorgji Trajkovski<sup>2,3</sup>, Pance Karagjozov<sup>2,3</sup>

<sup>1</sup>University Clinic for Traumatology, Orthopedic Diseases, Anesthesiology, Reanimation and Intensive care and Emergency department-Skopje,

<sup>2</sup>University Clinic for Digestive Surgery-Skopje,

<sup>3</sup>Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, R. North Macedonia

<sup>4</sup>Faculty of Medicine, Goce Delcev University in Stip, R. North Macedonia

### Abstract

In contrast to adults, SARS –CoV-2 mostly leads to a mild illness in children typically manifested with fever, cough and gastrointestinal symptoms.

The phenomenon of multisystem inflammatory syndrome in children (MIS-C) emerged during the coronavirus disease 2019 (COVID-19) pandemic. Children with MIS-C have current or recent exposure to the disease. Reported symptoms include fever or chills, tachycardia, gastrointestinal symptoms, rash, conjunctival injection and mucosal changes with a relative lack of severe respiratory disease.

We report a related case of a 15-year-old girl with signs and symptoms of MIS-C and respiratory failure. Multisystem inflammatory syndrome in children (MIDS-C) with respiratory failure is a serious life-threatening condition that requires treatment in an intensive care unit.

Invasive mechanical ventilation, invasive monitoring and treatment with combination therapy of antibiotics, corticosteroids, inotropic support, analgosedation, anticoagulation therapy and other lead to successful cure.

**Keywords:** coronavirus disease (COVID 19), children, multisystem inflammatory syndrome

### Introduction

In contrast to adults, SARS –CoV-2 mostly leads to a mild illness in children typically manifested with fever, cough and gastrointestinal symptoms. However, a few children have been reported to manifest severe disease which have been characterized by pneumonia, acute kidney injury, liver injury, metabolic acidosis, neurological injury, rhabdomyolysis, multisystem organ failure, and cardiac injury [1].

Post-COVID syndrome was described for the first time in spring 2020 in the context of a survey of prolonged COVID-19 symptoms, run by the Patient–Led Research Collaborative, citizens scientist group [2]. Soon after the first COVID-19 case evolved, they observed that COVID-19 patients had symptoms persisting for several weeks after acute infections.

The most common post-COVID symptoms include fatigue, dyspnea, olfactory and gustatory dysfunction, chest pain, myalgia, and sleep and mental disorders [2].

Carroll E *et al.* described a case of refractory status epilepticus (RSE) after recovery from acute COVID -19, likely secondary to a postinfectious inflammatory response [3].

The phenomenon of multisystem inflammatory syndrome in children (MIS-C) emerged during the coronavirus disease 2019 (COVID-19) pandemic. Children with MIS-C have current or recent exposure to the disease. Reported symptoms include fever or chills, tachycardia, gastrointestinal symptoms, rash, conjunctival injection and mucosal changes with a relative lack of severe respiratory disease. A large percentage of these patients develop shock and cardiac dysfunction, requiring intensive care unit level care. Laboratory results in children with MIS-C show severe inflammation [4].

We report a related case of 15-year-old girl with signs and symptoms of MIS-C, shock and respiratory failure.

### Case report

A 15-year-old patient with initials AR was referred from the Tetovo Clinical Center to our Clinic with abdominal pain and suspected appendicitis. The patient with severe hypotension and tachycardia was transported with an ambulance car. Anamnestic data for abdominal pain and lethargy 5 days before admission were obtained from the parents. Laboratory findings on admission: hemoglobin 105 g/l, erythrocytes 3.52 tpt/l, leukocytes 11.2 gpt/l, thrombocytes 198 gpt/l, natrium 132 mmol/l, kalium 3.5 mmol/l, chlorine 103 mmol/l, calcium 2.07 mmol/l, proteins 57 g/l, albumins 31 g/l, urea 8.5 mmol/l, creatinin 54 mmol/l, glucosis 5.38 mmol/l, LDH 304U/L, alt 39 U/l, AST 37 U/L, CRP 316.2 mg/l. Gas analyses: Ph 7.23, pCo2 6.26kPa, pO2 9.14 kPa, HCO3 19.4 mmol/l, Be -7.9 mmol/l, sPO2 90%, Lact 1.22 mmol/l. Hemostasis findings: thrombocytes 156 gpt/l, Hct 0.28%, PT 17 sec, APT 37.6 sec., TT 12.5sec, d-dimers 7838 ngr/ml, INR 1.5.

After the patient was examined by a digestive surgeon and anesthesiologist, she was admitted to the Digestive Surgery Room. Laparotomy was performed and serous ascites fluid was found without other pathology. Drainage was placed and an appendectomy was performed. Postoperatively the patient was admitted to the intensive care unit and placed on mechanical ventilation with continuous analgo-sedation. Therapy included: Imipenem 3x0.5g, Vancomycin 3x0.5 g, Fraxiparine 0.4 sc, Famosane 40 mg, Methylprednisolone 240 mg, Nacl 0.9% 1500 ml, Ringer 1500 ml, Gelofundine 500 ml, Adrenaline 2 mg / 50/2 ml / h continuously, midazolam 50 mg + fentanyl 30 ml / 50ml/2 ml / h continuous analgo-sedation and parenteral nutrition Cabiven 1250 ml / 50ml / h.

The patient was monitored by ECG, non-invasive arterial pressure, 24-hour diuresis, pulse, gas analysis and laboratory every day. A central venous catheter was inserted. Computer examination of the lungs and abdomen was made with the following finding: bilateral massive consolidations of the lungs and free fluid in the abdomen, without other pathological changes of other organs.

The patient underwent hemostasis and a serological test to detect antibody (COVID 19 antibody) that was positive for Ig 16 AU/ml, interleukin 6 was 144 pg/ml and procalcitonin 0.5 ng/ml. Laboratory results and the patient's clinical picture showed the presence of MIS-C, as evidenced by the positive IgG result of COVID 19, which indicated that the patient had undergone COVID 19 and consequently, had complications.

The patient continued to be treated on mechanical ventilation by reducing corticosteroid therapy, reducing and concluding adrenaline therapy, and reducing and excluding analog-sedation drugs. Intravenous antibiotics were given in full dose during the stay in ICU.

Enteral nutrition was included during this period. The patient's condition gradually improved, and there was an improvement in both laboratory and gas analyses.

On the ninth day of mechanical ventilation, the patient was extubated with adequate self-breathing and hemodynamically stable. After 5 days of extubation in good general condition, the patient was transferred to the Department of digestive surgery and from there discharged home.

### Discussion

In severe acute respiratory syndrome corona virus 2 (SARS-CoV2) infection the respiratory system is the main target organ; however, the gastrointestinal tract and the liver may also be involved, either symptomatically or with only laboratory derangements. The virus has been detected in respiratory secretions, feces and blood[5].

Some children have reported vomiting, nausea, diarrhea and abdominal pain during course of the disease. Diarrhea most often occurs during 1 - 8 days after the onset, with a median time of 3.3 days. Some patients had watery diarrhea as the first symptom[5].

On 28 April 2020, French clinicals alerted the French Public Health agency about an abnormal increase in cases of Kawasaki-like disease (KLD) and myocarditis in children requiring critical care support that occurred during of the ongoing coronavirus disease (COVID 19) epidemic in France.

Concomitantly, Riphagen *et al.* reported eight children displaying characteristics of hyperinflammatory shock, KLD or toxic shock syndrome and an Italian study reported additional children presenting with a KLD [6,7].

The epidemic curve of the PIMS (pediatric inflammatory multisystem syndrome) cases followed that of COVID-19 with a lag time of 4-5 weeks, supporting the hypothesis of PIMS being a post-infectious manifestation. The geographical distribution of the PIMS cases also correlated with that of the COVID-19 cases. The almost simultaneous detection of PIMS cases in three other places heavily affected by the SARS-CoV-2 epidemic (Italy, UK and US), further reinforces this hypothesis.

Conversely, the absence of identified PIMS cases in some countries may reflect a smaller COVID-19 epidemic, limited awareness of clinicals, a lack of a specific surveillance or system for KLD or other systematic inflammatory symptoms in children, additional risk factors in our population such as genetic factors or a combination of the above [8].

Most children with severe manifestations of COVID-19 recover completely. Accounting for access to diagnostic testing, children with underlying conditions appear to be most at risk for adverse outcomes.

The spectrum of outcomes was described among 48 children cared for in pediatric intensive care units (PICUs) in North America; 40 (83%) had an underlying medical condition. Although 18 (38%) of these children required mechanical ventilation and 1 patient required extracorporeal membrane oxygenation, the overall mortality was 4% among this North American cohort study [9].

As the pandemic progressed, the ability of SARS-CoV-2 infection to result in a broad spectrum of pathological conditions with varying clinical manifestations became apparent.

In April 2020, several European countries noted increasing numbers of children with systemic inflammation and clinical features that resembled both Kawasaki disease and toxic shock syndrome.

Simultaneously, reports from the United States began to describe the clinical characteristics, treatment, and outcomes of previously healthy SARS-CoV-2-infected children and adolescents with inflammation in multiple systems. Initially termed “the pediatric multisystem inflammatory syndrome potentially associated with COVID-19”, the CDC (Centers for Disease Control and Prevention) developed a case definition for what is now referred to as “multisystem inflammatory syndrome in children (MIDS-C)” in North America.

The clinical and laboratory parameters of children who meet the criteria for MIS-C differ from those with Kawasaki disease. Children with MIS-C are usually older, have more symptoms consistent with clinical shock, have involvement of gastrointestinal and cardiovascular symptoms, and have lymphopenia with notably elevated inflammatory markers [10].

This patient belongs to the group of older children and according to the symptoms and laboratory parameters had MIS-C. The patient had a good response to the therapy recommended by anesthesiology and intensive care specialists in ICU and she was completely cured.

## Conclusion

Multisystem inflammatory syndrome in children (MIDS-C) with respiratory failure is a serious life-threatening condition that requires treatment in an intensive care unit. Invasive mechanical ventilation, invasive monitoring and treatment with combination therapy of antibiotics, corticosteroids, inotropic support, analgesedation, anticoagulation therapy and other lead to successful cure.

## References:

1. Kohli U, Lodha R. Cardiac involvement in children with COVID -19. *Indian pediatrics* 2020; 57: 936-940. Maltezou C. Helena, Pavli A, Tsakris A. Post COVID Syndrome: An Insight on Its Pathogenesis. *Vaccines* 2021; 9: 497-509.
2. Carroll E et al. Post-COVID -19 Inflammatory Syndrome manifesting as Refractory Status Epilepticus. *Epilepsia* 2020; 61:e135-e139.
3. M.-K. Amato et al. Multisystem Inflammatory Syndrome in An Adult. *The Journal of Emergency Medicine* 2021. 1-3.

4. Matthai J. et al. Coronavirus Disease (COVID 19) and the Gastrointestinal system in Children. *Indian Pediatrics* 2020; 57:533-535.
5. Riphagen S. et al. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020; 395 (10237):1607-8.
6. Verdoni L. et al. An outbreak of severe Kawasaki-like disease at the Italian epicenter of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020; 395(10239):1771-1778.
7. Belot A. et al. SARS-CoV-2-related paediatric inflammatory multisystem syndrome, an epidemiological study, France, 1 march to 17 May 2020. *Euro Surveill* 2020;25(22): 2001010. doi: 10.2807/1560-7917.ES.2020.25.22.2001010.
8. Shekerdemian LS. et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr* 2020.
9. Shane A.L. et al. A Pediatric Infectious Diseases Perspective of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Novel Coronavirus Disease (Covid-19) in Children. *Journal of Pediatric Infectious diseases Society* 2020;9: 596-608.