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CASE REPORT

# COVID-19 in pediatrics: report of case of multisystemic inflammatory syndrome

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## Abstract

The novel coronavirus pandemic has brought significant impacts on the world population. So far, it is known that the disease has a greater impact in adults, while in pediatric patients it has milder manifestations. However, multisystem inflammatory syndrome in children (MIS-C), a serious and rare manifestation of SARS-CoV-2 infection, might affect children and adolescents. The new syndrome can manifest with a several signs and symptoms, ranging from non-purulent conjunctivitis, to shock and severe cardiac dysfunction, with characteristics similar to Kawasaki disease, incomplete Kawasaki, toxic shock syndrome, and macrophage activation syndrome. This case report aims to describe a case of MIS-C, its clinical evolution, the therapy used to treat the patient and, thus, assist healthcare professionals to recognize the characteristics and severity related to the syndrome. A 9-year-old female black child presented a clinical picture compatible with MIS-C, according to the Ministry of Health (Brazil). During hospitalization in a pediatric hospital, the patient developed cardiogenic shock and required care in the intensive care unit. Despite the similarity of MIS-C with other diseases that evolve with a systemic inflammatory response, it has some peculiarities, such as left ventricular dysfunction, one of the main manifestations, resulting in cardiogenic shock in most cases. The current treatment used is based on intravenous immunoglobulin and glucocorticoids. We emphasize the importance of conducting future studies to enable discoveries about the pathophysiological particularities of this new syndrome and enable the consolidation of an effective treatment.

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## INTRODUCTION

*Coronavirus disease* pandemic *2019* (COVID-19) brought significant impacts to the world population in various sectors, such as the economy. In this scenario, the socioeconomically vulnerable population, especially the black population, was the most negatively affected[1,2].

The disease severely affects adults over 60 years of age, mainly with chronic comorbidities[3]. Children and adolescents present milder manifestations, rarely develop severe respiratory diseases, with a significant portion of asymptomatic patients[4].

A new syndrome, called Pediatric Multisystem Inflammatory Syndrome (P-SIM), is being reported in pediatric patients infected with SARS-CoV-2[3,5]. It is known that most cases manifest with non-purulent conjunctivitis, acute gastrointestinal symptoms, cardiac dysfunction, among others. In addition, an elevation of inflammatory markers and a positive laboratory test for SARS-CoV-2 or a history of contact with a positive case are considered[2,6].

Coronaviruses are a large family of single-stranded RNA viruses. SARS-CoV-2, belonging to the β genus, is transmitted between humans through close contact with an infected person or through contaminated surfaces. In SIM-P, it is believed that neutrophils, through extracellular traps, can trigger inflammatory and immunological reactions in an uncontrolled manner, leading to an exaggerated systemic inflammatory response[4].

This research was approved by the Institution's Research Ethics Committee under opinion 38468620.7.0000.5361 and aims to describe a case of SIM-P, its clinical evolution, the therapy performed in order to help health professionals to recognize its characteristics and severity.

## CASE REPORT

ALF, 9 years old, female, black, previously healthy, came to the Emergency Care Unit (UPA) complaining of fever and loose stools, not bloody, for three days. A day ago, he evolved with prostration, tachypnea and conjunctival hyperemia. Symptomatic was prescribed, with improvement of fever, maintaining prostration and tachypnea. A chest X-ray was performed, with no changes. On examination, neck stiffness was evidenced, with no report of headache. It was decided to start empirical antibiotic therapy with ceftriaxone and transfer to a tertiary pediatric hospital for investigation.

In the emergency room, the clinical history showed that the patient had not taken recent trips, had no close contact with people with COVID-19 and that her vaccination schedule was up to date. On clinical examination, there was a good general impression, afebrile, but tachypnea, ocular hyperemia and neck stiffness. Laboratory tests were performed, with CRP of 191.6 mg/L, leukogram with left shift, CSF analysis without alterations, D-dimer of 3.08 ug/mL and erythrocyte sedimentation rate (ESR) of 65 mm (Table 1). Chest radiography showed infiltrate and perihilar bronchial thickening. Computed tomography (CT) of the skull was performed, without alterations. After initial analysis, there was suspicion of SIM-P and it was decided to maintain antibiotic therapy with ceftriaxone and to expand the spectrum of coverage with azithromycin.

The following day, after admission to infectious disease care, the team discontinued azithromycin and added clindamycin to the antimicrobial regimen. He also prescribed prophylactic anticoagulation with enoxaparin. An echocardiogram was performed with severe left ventricular systolic dysfunction – fractional shortening (FEnc) of 22% [Reference Value (RV): 28-44%]. Tests for SARS-CoV-2 were requested. In a new evaluation of the specialty, cardiogenic shock was found requiring transfer to the Intensive Care Unit (ICU).

In the ICU, he had a lowered level of consciousness and adrenaline and pulse therapy with methylprednisolone were started. New laboratory tests showed an increase in leukocytes, compared to the previous one, maintaining the shift to the left, as well as metabolic acidosis. After 24 hours in the ICU, tests for SARS-CoV-2 showed a negative polymerase chain reaction and a rapid serological test for total antibodies reagent. A CT scan of the chest (Figure 1) and abdomen was performed, showing bilateral pleural effusion, larger on the right, with a thickness of up to 1.1 cm; thickening of interlobular septa and prominent mediastinal and hilar lymph nodes; gallbladder mucosal thickening and hepatomegaly.

During hospitalization in the ICU, the patient received oxygen therapy and hemodynamic support, subsequently receiving an infusion of human immunoglobulin. After 36 hours of the first infusion, the patient persisted with fever, requiring repeat immunoglobulin. After this infusion, seven days after the onset of the condition, the fever improved. Additionally, he received filtered and irradiated red blood cell concentrate. In a new echocardiogram, four days after admission, there was an increase in FEnc to 31%, but still with significant left ventricular dysfunction. It was decided to suspend adrenaline and start dobutamine, administered for 24 hours, due to hypertensive peaks, with improvement after use. The patient progressed with improvement in the leukogram, but continued with an increase in D-dimer of 3.66 ug/mL (Table 1), thus, it was decided to maintain enoxaparin. Ceftriaxone and clindamycin were suspended, as well as pulse therapy with methylprednisolone and maintenance with prednisolone was started.

Patient remained in the pediatric ICU for seven days, evolving with clinical and laboratory improvement, being discharged to the care of Infectious Diseases. A new echocardiogram showed normal cardiac function (EFnc of 45%). Four days later, he evolved with a satisfactory clinical response, serial reduction of D-dimer and evidence of inflammatory activity, it was decided to suspend enoxaparin. He was discharged, with a prescription of corticosteroid

**Table 1.** Laboratory evolution during hospitalization of a patient with suspected Pediatric Multisystem Inflammatory Syndrome related to COVID-19, Florianópolis, Brazil, 2020.

| Exames | Emergency entrance | Cardiogenic shock | After immunoglobulin | Hospital discharge |
|---|---|---|---|---|
| **Hemoglobin** | 11.3 g/dL | 8.9 g/dL | 11.7 g/dL | 11.7 g/dL |
| **hematocrit** | 32.80% | 26.30% | 34.70% | 35.50% |
| **VCM** | 85 fL | 84.3 fL | 85.7 fL | 87.2 fL |
| **HCM** | 29.3 pages | 28.5 pages | 28.9 pages | 28.7 pages |
| **CHCM** | 34.5 g/dL | 33.8 g/dL | 33.7 g/dL | 33 g/dL |
| **RDW** | 12.70% | 13.60% | 13.40% | 13.20% |
| **leukocytes** | 12,500/mm³ | 20,600/mm³ | 14,300/mm³ | 9,130/mm³ |
| **platelets** | 152,000/mm³ | 222,000/mm³ | 182,000/mm³ | 391,000/mm³ |
| **INR** | 1.08 | 1.16 | 0.95 | NOT COLLECTED |
| **D-dimer** | 3.08 ug/mL | 1.05 ug/mL | 3.66 ug/mL | 1.29 ug/mL |
| **BNP** | NOT COLLECTED | 500 pg/mL | NOT COLLECTED | 10 pg/mL |
| **serum urea** | 30 mg/dL | 46 mg/Dl | NOT COLLECTED | NOT COLLECTED |
| **creatinine** | 0.5 mg/dL | 0.5 mg/Dl | 0.4 mg/dL | NOT COLLECTED |
| **PCR** | 191.6 mg/L | 189.1 mg/L | 89.2 mg/L | 3.1 mg/L |
| **VHS** | 65 mm | NOT COLLECTED | 39 mm | 44 mm |
| **troponin** | < 0.01 ng/mL | < 0.01 ng/mL | NOT COLLECTED | NOT COLLECTED |

Source: The authors (2020).



**Figure 1.** Computed tomography of the chest of a patient with suspected Pediatric Multisystem Inflammatory Syndrome related to COVID-19. The image shows bilateral pleural effusion, larger on the right, with a thickness of up to 1.1 cm. Florianopolis, Brazil, 2020. Source: The authors (2020).

therapy for gradual reduction. She remained hospitalized for 11 days, with negative blood, urine and cerebrospinal fluid cultures. Additionally, serological tests for Epstein-Barr, HIV, cytomegalovirus and toxoplasmosis were negative.

After discharge, outpatient follow-up at the tertiary pediatric hospital was recommended. Upon return, subsequent echocardiograms were within the normal range and laboratory tests were unchanged. Therefore, she was discharged from tertiary care, being referred to primary care.

## DISCUSSION

SIM-P is a clinical manifestation of SARS-CoV-2 in children and adolescents. Characterized by a systemic inflammatory response similar to Kawasaki disease (KD) and toxic shock syndrome, but with little pulmonary involvement – the main hallmark of COVID-19 in adults[7]. KD is an acute, febrile, self-limited primary vasculitis, with a predilection for the coronary arteries, preferentially affecting infants and young children[3]. In SIM-P, left ventricular dysfunction is the most common manifestation, with higher frequency in schoolchildren and adolescents[8,9].

According to the Ministry of Health, the case definition for SIM-P is: individuals hospitalized or who died aged between zero and 19 years; presence of high fever for three or more days; involvement of at least two organs (eyes, skin, cardiovascular system, among others); laboratory evidence of increased inflammatory markers; in addition to ruling out any causes of infectious origin; and evidence of SARS-COV-2 infection (laboratory or contact history with positive case/s)[6].

Radi et al.[8] carried out a systematic review, identifying 783 cases of SIM-P. Important particularities were pointed out: gastrointestinal symptoms occurred in more than 70% of the cases; all had fever; 68% required ICU; cardiovascular dysfunction was the most frequent abnormality; 77% required hemodynamic support with the use of vasoactive drugs and/or volume resuscitation; 94% showed increased inflammatory tests; pulmonary radiography showed alterations in 41%

of patients; only 1.5% died, demonstrating the importance of immunomodulatory treatment and its impact on the outcome[8]. The patient in the report presented several signs/symptoms, laboratory and imaging changes that corroborated the diagnosis of SIM-P and were also reported in the systematic review performed by Radia et al.[8] The clinical picture described fulfilled all the criteria of the Ministry of Health for SIM-P, being notified for this syndrome.

Studies try to find the basis of the immune response to SARS-CoV-2, in order to institute effective treatment. A study carried out with 48 patients showed that the immune response to COVID-19 is different in adults and children. While in children the immune response is predominantly carried out by antibodies of the IgG class, in adults it occurs by antibodies of all classes. As pediatric patients have an immune response mainly by IgG antibodies, it is believed that SIM-P manifests itself during the late stage of SARS-CoV-2 infection[7].

Another study, comparing patients with KD and SIM-P, showed that patients with SIM-P tend to be older, with the mean age for diagnosis of SIM-P being 11.4 years and 3.1 years for KD . Coronary involvement was more common in patients with KD. However, on echocardiography, patients with SIM-P had greater left ventricular dysfunction. The study concluded that the most recurrent finding in the acute phase of SIM-P is cardiogenic shock[9]. Recently, a study evaluated trends in the geographic and temporal distribution of US children with inflammatory syndrome during the COVID-19 pandemic, in which many patients developed shock, hypotension and approximately 60% required intensive care[10]. As described in previous studies, the patient in the present report also presented cardiac dysfunction that required intensive care with resolution of symptoms before hospital discharge. This outcome corroborates data from the publication by Feldstein et al., in which the resolution of most cardiovascular alterations was verified within 30 days[11].

Considering the global context, data from the US Centers for Disease Control and Prevention indicate that the proportion of Latino and black pediatric patients is slightly higher in those affected by the new syndrome, representing the largest proportion (73.6%) of those reported. Long-standing inequity in social determinants of health puts vulnerable populations at greater risk of COVID-19 and more severe disease, as with other neglected diseases[1,2].

The treatment for SIM-P is not completely established, but most cases recover with intensive care (ventilatory and hemodynamic support), intravenous immunoglobulin and glucocorticoids, considered the main treatments in the management of the syndrome[12].

The importance of the multidisciplinary team in the care and follow-up of the described case is highlighted. The therapeutic support with vasoactive drugs that the patient received, with a good response, was essential in the management, contributing to the timely institution of therapy, improvement of the clinical picture and satisfactory outcome.

## FINAL CONSIDERATIONS

We emphasize the importance of carrying out future studies that allow discoveries about the pathophysiological particularities of this new syndrome, given the limitations related to its recent discovery and the need for more robust scientific evidence.

## REFERENCES


1. Estrela FM, Soares CF, Cruz MA, Silva AF, Santos JR, Moreira TM, et al. Pandemia da Covid 19: refletindo as vulnerabilidades a luz do gênero, raça e classe. Ciênc Saúde Coletiva. 2020 Ago;25(9):3431-6.
2. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, et al. COVID-19 – associated multisystem inflammatory syndrome in children—United States, March–July 2020. MMWR Morb Mortal Wkly Rep. 2020 Ago;69(32):1074.
3. Alvim AL, Volpato AT, Sá Gomes EM, Cunha ET, Vilaça HM, Mayrink LB, et al. Síndrome inflamatória multissistêmica em crianças e adolescentes com COVID-19: uma revisão de literatura. J Infect Control. 2020 Sep;9(3):162-5.
4. Sociedade Brasileira de Pediatria (SBP). Síndrome inflamatória multissistêmica em crianças e adolescentes provavelmente associada à COVID-19: uma apresentação aguda, grave e potencialmente fatal. Rio de Janeiro: SBP; 2020.
5. Jiang L, Tang K, Levin M, Irfan O, Morris SK, Wilson K, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. Lancet Infect Dis. 2020 Nov;20(11):e276-e288.
6. Pereira MF, Litvinov N, Farhat SC, Eisencraft AP, Gibelli MA, Carvalho WB, et al. Severe clinical spectrum with high mortality in pediatric patients with COVID-19 and multisystem inflammatory syndrome. Clinics. 2020;75:e2209.
7. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Departamento de Imunização e Doenças Transmissíveis. Coordenação-Geral do Programa Nacional de Imunizações. Nota Técnica n. 16/2020-CGPNI/DEIDT/SVS/MS. Brasília (DF): Ministério da Saúde; 2020.
8. Weisberg SP, Connors T, Zhu Y, Baldwin M, Lin WH, Wontakal S, et al. Antibody responses to SARS-CoV2 are distinct in children with MIS-C compared to adults with COVID-19. Nature. 2020 Nov;22:25-31.
9. Radia T, Williams N, Agrawal P, Harman K, Weale J, Cook J, et al. Multi--system inflammatory syndrome in children & adolescents (MIS-C): a systematic review of clinical features and presentation. Paediatr Respir Rev. 2020 Jun;38:51-7.
10. Belay ED, Abrams J, Oster ME, Giovanni J, Pierce T, Meng L, et al. Trends in geographic and temporal distribution of US children with multisystem inflammatory syndrome during the COVID-19 pandemic. JAMA Pediatr. 2021 Ago;175(8):837-45.
11. Feldstein LR, Tenforde MW, Friedman KG, Newhams M, Rose EB, Dapul H, et al. Characteristics and outcomes of us children and adolescents with multisystem inflammatory syndrome in children (MIS-C) compared with severe acute COVID-19. JAMA. 2021 Mar;325(11):1074-87.
12. Matsubara D, Kauffman HL, Wang Y, Calderon-Anyosa R, Nadaraj S, Elias MD, et al. Echocardiographic findings in pediatric multisystem inflammatory syndrome associated with COVID-19 in the United States. J Am Coll Cardiol. 2020 Out;76(17):1947-61.