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PEDIATRIC MULTISYSTEM INFLAMMATORY SYNDROME (MIS-C) ASSOCIATED WITH COVID-19 IN A CHILD FROM THE WESTERN AMAZON

Luiz Felipe Campos

Judith Barroso de Queiroz

Abstract: Goal: Contribute to the knowledge of medical society by identifying the disease and understanding its importance, especially from the point of view of clinical and laboratory diagnosis, with emphasis on clinical manifestations. **Methods:** The proposed study is a case report, observational and descriptive, developed at Hospital Pronto Socorro da Criança Zona Sul, started in February 2021. The instruments used to collect information were anamnesis and physical examination. during the period in which the patient remained hospitalized in the referred hospital unit - by means of a medical record review. The observation and discussion of the case in the service's multidisciplinary meetings were also part of the data acquisition. The completion of the collection of information took place through the acquisition of secondary data with continuous review of the medical record and photographic record of the diagnostic methods to which the patient was submitted and literature review (until October 18, 2022 in the databases of the PubMed/MedLine with the keywords of this work). All records and information obtained were duly explained and requested from the patient's legal guardian, who by mutual agreement and non-profit signed a free and informed consent form (ICF). **Experience report:** To reinforce, through a case report, the importance of the clinical manifestations and complementary tests of MIS-C in a child from the Western Amazon and to describe the treatment instituted and the recommended clinical follow-up**. Conclusion:** Pediatric multisystem inflammatory syndrome was reported in Brazil during the second wave of the COVID-19 pandemic and the importance of such a serious disease requires studies and publications of similar cases in order to identify the factors involved in the etiology of the disease and create a database for correlations of cases and treatments instituted.

Keywords: Inflammation, Mucocutaneous lymph node syndrome, cardiogenic shock, Coronavirus infection.

INTRODUCTION

The first case report of a 6-month-old child with Kawasaki disease (KD) and COVID-19 was published in the United States on April 7, 2020. Since that first report, countries with SARS-CoV- 2 have reported more cases of this syndrome, called pediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (MIS-C), which shares clinical and laboratory characteristics of Kawasaki disease (typical or incomplete), staphylococcal toxic shock syndrome and streptococcal, bacterial sepsis and macrophage activation syndrome. MIS-C usually affects children over 5 years of age, predominantly Afro-descendants in most studies, and has a higher incidence of cardiac changes. The hypothesis of a possible temporal association with SARS-COV-2 infection was raised, because some of the children were positive for SARS-CoV-2 by polymerase chain reaction (RT-PCR) or serology. These children have a prolonged high fever, rash, and prominent gastrointestinal symptoms in 50-60% of cases (abdominal pain, non-bloody diarrhea, ascites, and ileitis), conjunctivitis, lymphadenopathy, irritability, and headache. Some severe cases present with shock due to cardiac dysfunction, with or without myocarditis or coronary artery aneurysm. Respiratory symptoms may be present, usually caused by concomitant shock. In this article, we describe a case report of a 6-year-old Amazonian child, using clinical and laboratory data of this intriguing syndrome to alert pediatricians and guide the diagnosis and management of these patients.

METHODS

The proposed study is a case report, observational and descriptive, developed

at the Hospital Pronto Socorro da Criança Zona Sul, started in February 2021. The instruments used for the collection of information were the anamnesis and physical examination in the period in which the patient remained hospitalized in the referred hospital unit - by means of a chart review. The observation and discussion of the case in the service's multidisciplinary meetings were also part of the data acquisition. The completion of the collection of information took place through the acquisition of secondary data with continuous review of the medical record and photographic record of the diagnostic methods to which the patient was submitted and literature review (until October 18, 2022 in the databases of the PubMed/MedLine with the keywords of this work). All records and information obtained were duly explained and requested from the patient's legal guardian, who by mutual agreement and non-profit signed a free and informed consent form (ICF).

CASE REPORT

A 6-year-old child was admitted to the emergency department of the Hospital Pronto Socorro da Criança Zona Sul, with a history of six episodes of uncontrollable vomiting, without the presence of food remains, five episodes of watery diarrhea without blood, or pus, measured daily fever of 39 degrees Celsius, productive cough and abdominal pain starting six days after admission. He looked for optional, was diagnosed with bacterial tonsillitis, was discharged with Amoxicillin with Clavulanate for 4 days. Two days ago, the clinical picture worsened with worsening of the abdominal pain, emergence of a non-scaling craniocaudal maculopapular rash, left unilateral cervical lymphadenopathy and bilateral purulent conjunctivitis. Due to the worsening of the condition, he was admitted to the Emergency Room in a critical condition, tachydyspneic, pale, dehydrated, with pain facies, conjunctival hyperemia, fever of 38 degrees Celsius and maintenance of abdominal pain. He denied infectious diseases and immunization in the 30 days prior to attendance. He also denied weakness in the upper or lower limbs, lymph node enlargement, headache and scaling of the extremities. Reported contact with confirmed COVID (grandmother) sixty days after admission.

On physical examination: regular general status, active and reactive, pain fascies, dehydrated, acyanotic, anicteric, pale ++|++++, hemodynamically stable, isochoric pupils, preserved direct and consensual photomotor reflex, eudiadochokinesia, bedridden, Grade 4 muscle strength (Medical Research Council) in foot extensors and flexors and in thigh flexors and extensors, upper limbs: Grade 5 muscle strength with preserved range of motion motor reflexes (triceps, biceps, styloradial, patellar and Achilles) and sensitivity preserved (deep: postural kinetic and superficial: pain and general sensitivity).

Normal admission exams (blood count, sodium, potassium, magnesium, calcium, phosphorus, chlorine, total bilirubin and fractions, type 1 urine), rapid test for Covid IgM and non-reactive serum IgG, VDRL, anti-HiV ½, HbSAg and anti - HBS negative. And altered inflammatory tests and tests related to multisystem inflammatory response syndrome (D-dimer: 5.48mg/L, ESR: 89mm, CRP: 192 mg/L, Triglycerides: 291 mg/dl, creatinine: 0.2 mg/dl, urea: 15 mg/dl, albumin: 2.6 g/dl, TGO: 70U/L, TGP: 73 U/L). AP chest X-ray in bed with cardiomegaly and cephalopulmonary tract cephalization, ECG: normal. The patient was admitted.

During hospitalization, he manifested worsening of abdominal pain, with maintenance of watery diarrhea, tachypnea

(RR: 46 bpm), dyspnea (nasal flaring), worsening of respiratory auscultation (bullous crackling rales in both hemithoraxes) and hemodynamic instability. He needed vasoactive drugs, systematic analgesia with medium-potency opioids, dual-schedule and broad-spectrum antibiotic therapy and, finally, human immunoglobulin (IVIG) and acetylsalicylic acid at the doses recommended by the Brazilian Society of Pediatrics.

An investigation was carried out with Doppler echocardiography, which showed mild LV systolic dysfunction with an ejection fraction of 52% (Teicholz) and mild mitral and tricuspid valve regurgitation, PASP: 30 mmHg, normal anatomy. The pediatric cardiologist suggested starting vasoactive drugs (Dobutamine at 10 cmg/kg/min, avoiding fluid overload, avoiding anemia and reassessing with a new echocardiogram in six days. Thick blood smear was also requested for Malaria with a negative result.

After 48 hours of admission and, consequently, of the infusion of human immunoglobulin, he evolved with progressive improvement of bilateral purulent conjunctivitis, cervical lymphadenopathy, abdominal pain, diarrhea, craniocaudal rash, tachydyspnea and, mainly, hemodynamic instability, being discharged by the hospital team. emergency room for follow-up in the ward of the multisystem inflammatory condition, being monitored by the pediatric and pediatric cardiology team. After 6 days of hospitalization, he was discharged in good general condition and with all physiological functions preserved and normal.

DISCUSSION

In 2020, MIS-C cases in Brazil had an average age of five years, most occurred in brown, male children, after the peak of COVID-19 in the pediatric age group. The clinical manifestations found were diverse and are associated with elevation of inflammatory markers, coagulopathies, multiple organ dysfunction and positive serology for SARS-CoV-2. The case fatality rate was 6.4% in patients with oxygen saturation below 95% and with elevated urea in laboratory tests.

Gastrointestinal symptoms, which were present in the evidenced case report, were reported in a study on MIS-C at Kings College London, in 553/783 (71%) of cases, including abdominal pain in 285/783 (36%), diarrhea in 214/783 (27%) and vomiting in 196/793 (25%). Regarding cutaneous manifestations, with variable description, 330/783 (42%) of the cases were reported. Fever, a key criterion in the definition of MIS-C, was presumed to be present in all 783 cases. Respiratory tract symptoms, in disagreement with the patient described, were present in a minority of cases, 35/783 (4.5%).

The renal changes found may be related to a combination of hypovolemic and hyperinflammatory shock. Although the pathophysiology of MIS-C has not been fully elucidated, it is believed that multiple organ failure occurs due to an exacerbated delayed immune response, and not necessarily to the direct action of the virus on tissues.

Circulatory/hemodynamic system complications have been shown to be more frequent in MIS-C than in Kawasaki Syndrome and, although there is a risk of sequelae, a good prognosis has been observed.18 These complications have also been observed in severe and fatal outcomes of COVID-19 in adults, and may be associated with myocardial impairment due to the phenomenon known as 'cytokine storm', as well as progression of acute respiratory failure.18 Changes in cardiac function biomarkers and hyperinflammatory reaction have been reported as predictors of MIS-severity C, but were not included in the study of association with death due to lack of data.

In Brazil, the therapy used in cases of MIS-C was varied, which may be related to nonspecific pathophysiological manifestations, absence of a clear prognosis and the possibility of life-threatening. However, there is no standardized treatment for MIS-C in the literature. Treatment protocols have been proposed, based on clinical management guidelines for other inflammatory syndromes with a similar clinical spectrum. The use of anticoagulants is indicated in cases of thromboembolic events and plays an important role in the prevention of shock. The results found suggest that immunoglobulins and anticoagulants may have been protective factors against a fatal outcome; the results, however, must not be viewed as measures of efficacy, given the observational nature of the study.

CONCLUSION

Pediatric multisystem inflammatory syndrome has been reported in Brazil and the importance of a disease as rare as MIS-C requires studies and publications of similar cases in order to identify the factors involved in the pathophysiology of the disease and create a database for correlations of the cases found in pediatrics and the treatments instituted.

The ideal pharmacological therapy needs to be validated. In principle, each service, in different parts of the world, has behaved similarly, although not always the same, based on the clinical picture expressed in each patient and its severity. In cases presenting with diagnostic criteria of classic KD, usual therapy with intravenous gammaglobulin (IVIG) and acetylsalicylic acid (aspirin) has been indicated.

IVIG must be prescribed at a dose of 2g/kg with prolonged infusion over 10-12 hours. It can be divided into 2 or more days, depending on the patient's hemodynamic conditions.

Aspirin can be used at a dose of 80-100mg/kg/day as a non-steroidal anti-inflammatory drug initially, changing to a dose of 3-5mg/kg/day (antiplatelet dose) after fever defervescence2. Many services recommend a lower initial dose of aspirin, 30-50mg/kg/day, while others recommend a dose of 3-5mg/kg/day from the beginning, since there seems to be no change in the evolution and prognosis of children. with Kawasaki disease with low, moderate or high dose of the drug. The wide variety of combinations used to date clearly requires a large registry, probably worldwide, to provide answers as to which patients are eligible for treatment, and how to properly treat them, without unnecessary or ineffective interventions.

Evidence of COVID-19 (RT-PCR, antigen, or serology) or probable contact with COVID-19 patients is required.

The risk of hemodynamic instability followed by cardiogenic shock is a present threat for patients with MIS-C and in this perspective, the different clinical and laboratory manifestations of this disorder must be recognized and studied. The severity of the disease is of significant importance for the patient and his family, and a longitudinal study of the reported case and family members is necessary to recognize determining factors in the worsening or control of symptoms.

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