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Annals of Pediatrics & Child Health

Review Article

Association of Myocarditis with Covid-19 in Children

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Submitted: 12 January 2022

Accepted: 05 February 2022

Published: 08 February 2022

ISSN: 2373-9312

Keywords

- Coronavirus
- Myocarditis
- Multisystem inflammatory syndrome in children
- COVID-19

Abstract

Introduction: With the advent of the SARS-CoV-19 pandemic in late 2019, several cases of virus-related myocarditis are emerging. In regard to the pediatric population, such cases were related to the MIS-C, which usually manifested about three weeks after viral infection. In this literature review article, we aim to summarize the relation between a coronavirus infection and myocardial involvement in childhood, its prevalence and clinical follow-up.

Methodology: A non-systematic review was carried out focusing on the myocarditis, COVID and Multisystem inflammatory syndrome in children, an overview of epidemiology, identification and management. The research was made from classic books of literature as well as recent articles from the last year. The online databases (Google Scholar, Medline, PubMed and Scielo) were consulted using terms such as "covid", "coronavirus", "SARS-CoV-2", "myocarditis", "multisystem inflammatory syndrome" and "Kawasaki like". This article discusses the myocarditis, the definition, etiologies, epidemiology, clinical characteristics, diagnostic, complications and Association between COVID-19 and myocarditis.

Final considerations: It is necessary to understand that the diagnosis of myocarditis is a challenge due to its nonspecific and highly variable clinical manifestations. However, it is essential that the clinician be able to suspect and diagnose myocarditis early, in order to avoid progression to irreversible complications and high mortality. Finally, it is concluded that additional studies are necessary for a better understanding of the pathophysiology involving the new coronavirus and myocyte injury, as well as further clarification regarding the therapeutic approach for the affected children.

ABBREVIATIONS

COVID-19: Coronavirus Disease 2019; MIS-C: Multisystem Inflammatory Syndrome in Children; SARS-Cov-2: Serious Acute Respiratory Syndrome Coronavirus 2; WHO: World Health Organizations

INTRODUCTION

Myocarditis is an inflammatory disease that affects the myocardium and its prevalence is still undefined, although it has severe acute and chronic complications. Its fatal complication, sudden death, is responsible for about 20% of all occurrences of this pathology in childhood [1]. In addition, this disease can lead to arrhythmias and even heart failure due to irreversible dilated cardiomyopathy [1].

Viral infection is the most prevalent cause of myocarditis, especially coxsakievirus B [1]. However, given the current situation of the pandemic this pathology has been gaining prominence due to new virus and, consequently, more cases of myocarditis have been reported [2,3].

This pandemic caused by SARS-CoV-2 began in December 2019, has had a catastrophic effect on the world, resulting in more than 3 million deaths worldwide and 130 million cases [2-4]. In general, it is observed that in the pediatric population the cases are asymptomatic or have a mild picture when compared to those in the adult population [2-6]. Despite this, many countries are reporting the occurrence of an event called MIS-C associated with COVID-19. It is reported to appear about. This syndrome to appear about a few weeks after the onset of COVID-19 in children and adolescents due to an intense immune response [2-6].

Some aspects of this emerging pediatric disease are similar to those of Kawasaki disease, in addition to it affects multiple organs and can lead to shock [2-6]. It is important to mention that the development of myocarditis in the inflammatory syndrome has occurred in more than half of the cases [2,3,6]. This is explained

by the virus' affinity for endothelial cells and the myocardium, leading to cardiac inflammation, dilated cardiomyopathy and tissue fibrosis [7,8].

Within this theme, the objective is to carry out a literature review of information that may be useful for understanding the cardiac implications in the form of myocarditis after SARS-CoV-2 infection in pediatric patients, paying attention to possible sequelae.

MYOCARDITIS

A good understanding of myocarditis and its complications are of paramount importance for the health professional who deals with the pediatric population. Then, myocarditis is defined as an inflammatory disease of the heart muscle [9]. It is characterized by histological evidence of inflammatory infiltrates, localized or diffuse, within the myocardium associated with myocyte degeneration and necrosis of non- ischemic origin [9,10]. This disease has a wide variety of clinical presentations, which often confuses it with other pathological processes due to the diagnosis of myocarditis is a challenge [11].

EPIDEMIOLOGY

The actual incidence and prevalence of myocarditis in the pediatric population is difficult to estimate, because the disease has a subclinical presentation or just unspecific symptoms, which can be misinterpreted [11,12]. In addition, endomyocardial biopsy (confirmatory examination of myocarditis) is not routinely performed in clinical practice [11,12]. Necropsy studies suggest an approximate incidence of 0.12 and 12% [11,12]. Myocarditis was also associated with 1.8% of all deaths, besides being responsible for 16 to 20% of cases of sudden death in childhood [9]. Studies show a predominance of cases in males and a higher frequency in children under two years of age, who have a worse prognosis [11,12].

ETIOLOGIES

Viral infections represent the main etiology of myocarditis, but it can also be caused by bacteria, protozoa, autoimmune diseases, toxins, among others [11]. The most common cardiotropic viruses are adenovirus, enterovirus, parvovirus B19 and herpes simplex. Coxsackie B virus is recognized as the most common etiologic agent. However, recent studies have shown a greater number of cases caused by adenovírus [11].

Drugs can induce myocarditis both by direct toxicity to the myocardium and by induction of hypersensitivity and are associated with eosinophilic myocarditis [11].

VIRAL PATHOPHYSIOLOGY

Cardiac involvement secondary to viral infection occurs in some phases [9, 11, 13]. At first, there is invasion of the myocardium by the cardiotropic vírus, that enters the cardiomyocyte through specific receptor-mediated endocytosis [11,13]. Subsequently, there is rapid viral replication within the cell, myocyte necrosis and apoptosis [9]. In this first moment, tissue damage results from the direct action of the virus on the cell, and not from the autoimmune response [11]. In the second moment, there is activation of the immune system with recruitment of natural killer cells, macrophages and activation of CD4 T lymphocytes, resulting in an increase in pro-inflammatory cytokines and B lymphocytes [13]. These infected cells are destroyed, causing even more damage to the myocardium and inflammation [13]. In addition, there is the production of autoantibodies against structural and mitochondrial proteins [13].

When B lymphocytes are activated, they produce antibodies that can react with myocardial antigens, contributing to the impairment of the contractile function of the heart [11]. In the third stage, there is viral elimination and recovery, or disease progression [9]. Myocardial injury can persist in the last phase, leading to the development of fibrosis and ventricular remodeling, with dilated cardiomyopathy [13]. In the post-viral phase, the immune response continues even after the virus is cleared [11].

CLINICAL MANIFESTATIONS

The clinical manifestations of myocarditis are generally nonspecific and quite variable. They can range from asymptomatic to sudden death [9]. Some patients may have viral prodromes such as fever, myalgia, nausea and vomiting, abdominal pain and loss of appetite [9,13]. Other possible symptoms are fatigue, decreased tolerance for physical activity, palpitations, and syncope [9,11]. The most common manifestations found in children with myocarditis include tachycardia, dyspnea, and anorexia.

Myocarditis can also resemble an acute coronary syndrome, with typical chest pain independent of breathing, ST-segment elevation and increased cardiac enzymes [9,12,16]. This condition, although present in a minority of cases, when it occurs, it is related to older children and manifests itself due to pericardial irritation [14,15].

COMPLICATIONS

The outcome of myocarditis is dependent on multiple factors, such as severity of presentation, degree of specific aggressiveness for each etiology, expertise of the medical team, location and time of instituting the treatment when it is necessary [9,10]. However, most of the children progress favorably, with full recovery and no long-term sequelae [15].

The main complication of the disease is the progression to dilated cardiomyopathy and severe heart failure, due to damage to myocytes in response to a possible etiologic agent, the most commonly being viruses [10,12,16]. In cases of dilated cardiomyopathy, the mortality rate it can affect 46% of patients and the need for heart transplantation reaches 31% of them [15]. Another related complication is the development of arrhythmias [11,17]. However, it is important to report that such morbidities are not fully defined for the various etiologies of the pathology [11,17].

The persistence of cardiotropic virus leads, in patients with decreased left ventricular function, to the need for specific treatment to preserve this function [9]. As for the electrocardiographic findings, presence of Q wave, left bundle branch block and QRS duration greater than 120 milliseconds is associated with higher rates of heart transplantation and death [15,18]. Atrioventricular block recovery rates in one week are variable, around 67%, so that persistence beyond

seven days indicates the implantation of permanent pacemaker in cases of advanced blocks [9,12,19]. Other worse prognostic factors include NYHA grade IV dyspnea, elevated troponin I, increased brain natriuretic peptide, moderate or severe mitral regurgitation, tachyarrhythmias, and ejection fraction less than 30% [12,15,16].

Cases of fulminant myocarditis are more likely to evolve to dilated cardiomyopathy [17]. When manifested through severe hemodynamic compromise, mortality in neonates and children under one year of age reaches more than 75% of cases [11]. Historically, it has been shown that mortality in the fulminant form is lower after resolution of the critical phase. However, recent questions dispute this assertion, since the studies carried out to date have a small sample and the most aggressive courses of the disease may be being omitted [9].

As for treatment modalities, it is known that children on the list of heart transplants for myocarditis are more severe than others who need the organ for other reasons. Thus, they have risk factors for unfavorable outcomes after the procedure, such as renal dysfunction, mechanical ventilation and acute rejection of the transplanted organ [9,11]. Finally, cases that affect females requiring extracorporeal membrane oxygenation (ECMO), dialysis and presence of arrhythmia are associated with high mortality [11].

DIAGNOSTIC

The diagnosis of myocarditis is challenging, as there is no well-established consensus for it, and even the treatment and follow-up of patients with this pathology are still uncertain [12,17,19].

In general, the investigation consists of anamnesis and physical examination, electrocardiographic and cardiac biomarker abnormalities, as well as changes in imaging exams. However, these patterns may be absent in patients with subclinical myocarditis (which occurs in most children), the diagnosis goes unnoticed by the medical team and case resolution tends to be spontaneous [9,12,14].

The non-specific nature of the symptoms leads to a delay in diagnosis, which can be fatal, as it provides an advance of the disease, which ends up being recognized only during necropsy due to unexpected death [11,15,16,20]. Weber et a. concludes in their study that up to 2% of pediatric deaths in a British center had histological signs of myocarditis during necropsy [20]. Therefore, it is established that this is a highly underdiagnosed pathology despite the significant morbidity and mortality in the pediatric population [15,20].

Therefore, myocarditis should be considered in every previously healthy child with complaints, signs and symptoms indicative of the onset of heart failure [10,20].

a) laboratory tests: Infectious and non-infectious causes can be investigated through specific laboratory tests for each etiology, including serology, polymerase chain reaction (PCR) of the histological sample and imaging tests [9,10,17]. Microbiological culture helps in the identification of pathogens causes of myocarditis in the bloodstream, respiratory tract, urinary and rectum, although it is common not to identify the agents in such cases [20]. Viral etiologies manifest lymphocyte predominance in the blood count [10,22].

On the other hand, inflammatory markers such as C-reactive protein and ESR are commonly elevated9 [12,17,20]. AST elevation is observed, with 85% sensitivity [14,15,17]. Nevertheless, ALT usually has normal serum levels in the face of disease. B- type natriuretic peptide (BNP) is increased due to ventricular enlargement and stretching of myocytes in the course of the pathology, although nonspecific [17].

Cardiac biomarkers aid in diagnosis, but cannot be used as single markers for definitive diagnosis due to their low specificity. In addition, they are usually present in a smaller proportion of cases [9,18]. Both troponin T and I are found in higher serum levels, but the second is more specific for myocarditis and is positive in about a third of patients with confirmation of disease by biopsy [10,17,22]. However, as evidenced by Eisenberg et al., troponin T levels below 0.01 ng/mL exclude the diagnosis of myocarditis in children without previous heart disease [17].

b) Electrocardiogram: Electrocardiographic changes have a high positive predictive value but a low negative predictive value. There are nonspecific ST-T wave changes, ST segment elevation, sinus tachycardia with low-voltage QRS complexes, atrioventricular conduction delays, axis deviation and ventricular hypertrophy [9,10,12,14,15,18,19,21,22]. It is still possible to find abnormal Q waves, negative T waves, widened QRS and prolonged PR interval [9,11,17,20]. Thus, it is concluded that viral myocarditis can cause atrial, ventricular arrhythmias, atrioventricular blocks and infarct-like electrocardiographic patterns [10,14,15,18,22].

Arrhythmias associated with myocarditis range from premature contractions to partial or complete atrioventricular block [9,12,18,19]. Therefore, in patients with recent onset of third-degree atrioventricular block, myocarditis should be investigated and excluded [12]. Regarding the infectious etiology, more specifically the viral, the observed arrhythmias usually consist of atrial ectopic tachycardia, atrial flutter and third-degree atrioventricular block with syncope and ventricular tachycardia [21].

c) Echocardiogram and chest X-ray: Echocardiography together with chest X-ray are the first imaging tests to be performed in the investigation of myocarditis [17]. Although the echocardiogram does not provide a diagnosis when used alone, in most cases it presents some abnormality and is one of the main evaluation methods [9,17,22]. In addition, when performed in series, it is the method of choice to follow the evolution of the disease, being able to make it possible to exclude endocardial fibroelastosis, coronary anomalies, hypertrophic and restrictive cardiomyopathy, and other pathologies associated with heart failure (such as valvular defects, congenital and amyloid heart disease) [10,15,18,22].

Echocardiographic changes in patients with mild clinical manifestations may be normal. When any abnormality is present, they are nonspecific [17]. In myocarditis, it is possible to observe global left ventricular or biventricular dysfunction, dilated cardiomyopathy, reduced left ventricular ejection fraction, mitral and tricuspid regurgitation, atrial enlargement,

pericardial and/or pleural effusion, ventricular and atrial thrombosis [9,12,17,21.22]. Although the right ventricle has less involvement, its evaluation by echocardiography is essential to predict the outcome, since the probability of death and the need for heart transplantation is greater in patients with change in said cardiac chamber [3,10,12,18,22].

Interesting fact found by ultrasound examination, it is possible to differentiate classic acute myocarditis from fulminant myocarditis. While in the former there is an increase in diastolic dimensions with normal septal thickness, the latter presents with a lower ventricular ejection fraction, normal left ventricular size and increased septal thickness. Furthermore, fulminant myocarditis has a greater association with the history of recent previous viral infection, so that the manifestations of severe and sudden heart failure occur after two to four weeks [9,12, 16-18].

The prevalence of abnormal chest X-rays is about 60 to 90% with myocarditis. Findings include cardiomegaly, pulmonary congestion, interstitial infiltrate, pleural and pericardial effusion [14,16,19,20]. However, cardiac dimensions may be normal in cases of fulminant myocarditis [18]. Chong et al. concluded that there are five discriminating symptoms and signs of myocarditis, such as dyspnea, hypotension, impaired perfusion, electrocardiographic abnormalities, and chest X-ray changes. Three or more positive criteria out of the five are indicative of high probability for the disease [17].

d) Magnetic resonance imaging and nuclear medicine: The diagnosis of myocarditis using cardiac magnetic resonance with gadolinium contrast is the gold standard among non-invasive methods, achieving a sensitivity of 100% and a specificity of 90%. The image provides visualization of tissue damage through edema, hyperemia, necrosis and fibrosis. The recently revised Lake Louise diagnostic criteria are used in this method [9,12,14,19]. When combined with non-invasive molecular analysis techniques, it allows detecting and staging viral myocarditis, in addition to enabling monitoring of the evolution of myocardial lesions [14,15,22]. Therefore, the best non-invasive way to assess the clinical picture of myocarditis is the aforementioned exam and serial echocardiography [19]

Another advantage of magnetic resonance imaging is the detection of focal myocardial lesions that commonly go unnoticed on biopsy, in addition to allowing the collection of material for histological study to be guided, thus improving the method's sensitivity [10,18,22]. However, it is important It should be noted that the ideal time to perform cardiac magnetic resonance is still in the acute phase of the disease, since after two weeks the myocardial edema begins to regress and the tissue enters the recovery phase. As a result, the sensitivity of the exam is impaired during this period [9]. Furthermore, magnetic resonance imaging allows a differential diagnosis between myocarditis and coronary ischemia. Examination findings related to worse outcomes include global hypokinesia, left ventricular dilatation, left ventricular ejection fraction less than 30%, and transmural myocardial involvement [14,15].

Another diagnostic tool was developed more recently with the advent of nuclear medicine. To make the images, gallium-67 and monoclonal antibodies against the myosin present in the heart muscle marked with indium-111 are used. Nevertheless, in asymptomatic patients such scans may simply be examination findings [10,22].

e) Endomyocardial biopsy: Performing an endomyocardial biopsy is the gold standard for diagnosis [9,10,12]. However, it is essential to analyze the risk-benefit ratio of the procedure due to the complications of sedation and anesthesia. Among the complications of the biopsy, catheter injury, prolonged bleeding, arrhythmias, tricuspid valve injury, ventricular perforation, pneumothorax, hemothorax and death are cited [11,12,14,15,18,20]. Therefore, the method is contraindicated in children with decompensated heart failure and in the presence of intracavitary thrombi [10]. Among the indications for its performance, there are cases of recent onset heart failure less than two weeks with hemodynamic compromise regardless of left ventricular dilatation, ventricular arrhythmias, atrioventricular block of high grade and ineffective response to treatment after one to two weeks [11,12,18].

The Dallas criterion is the pathological definition of myocarditis, which postulates that the presence of inflammatory infiltrate associated with necrosis or damage to myocytes not characteristic of an ischemic event due to coronary disease is necessary [9,10,12,17,19,20]. Thus, it is observed in the biopsy material infiltrated mononuclear cells above 14 cells/mm2 and increased expression of human leukocyte antigen (HLA) molecules of class II [11,12,18]. It is still possible to have infiltration of leukocytes, monocytes and macrophages. In rarer cases, multinucleated giant cells and eosinophils dominate the inflammatory process [11]. The prediction of risk of death or heart transplantation can be performed through the presence of inflammation stained by immunoperoxidase [18].

In addition to the biopsy allowing evaluation of the extent of the inflammatory process and fibrosis, it helps in the differential diagnosis of storage diseases and mitochondrial abnormalities [10,22]. Another advantage of the method is the identification of cardiotropic viruses by performing PCR on the extracted samples, leading to the detection of the etiologic agent in 24 to 41% of patients [9,14,15]. However, possible errors when collecting the material on which the biopsy will be performed and variability in the interpretation by pathologists make the method less sensitive, so that resonance Cardiac magnetic resonance is gaining more and more prominence to replace such an invasive method [10,14,16,18]. Despite the limitations, immunohistochemical techniques allow better detection of inflammation in the samples [11,12,18]. It is estimated that for the method under discussion to reach a sensitivity of 80%, around seventeen samples are needed due to the uneven distribution of lesions in the myocardium, which makes its r achievement [18].

COVID-19

In December 2019, the outbreak of a new disease, COVID-19, began in Wuhan, Hubei province, China [23]. The disease is caused by the severe acute respiratory SARS- CoV-2. This virus causes COVID-19, which has spread to 192 countries, affecting individuals of all age groups, with about 130 million reported cases and almost three million deaths as of the date of this literature review [24]. Countries still struggle with the burden on

health systems and the socioeconomic consequences resulting from the ongoing pandemic [25].

The transmission of SARS-CoV-2 occurs through close contact with symptomatic or asymptomatic people through respiratory droplets, contaminated surfaces or by aerosols in poorly ventilated spaces and agglomerations [23]. Virological studies show that the virus has its highest concentration in the respiratory tract. higher at the beginning of the infectious process, which presents an incubation period from the exposure, with an average of five to seven days, which may extend up to fourteen days [23].

The infectious picture caused by COVID-19 has three stages, progressing together with severity [25] The first stage is characterized by symptoms similar to those of an upper airway infection [25] Subsequently, a portion of patients progress to the second stage described. such as viral pneumonia, which may require hospitalization and mechanical ventilation [25]. Still in the second stage, pulmonary inflammation may overlap with coagulopathy [25] Increased inflammation markers (C-reactive protein, ferritin, IL-6 and D-dimer) in the second stage are associated with progression to acute respiratory syndrome and poor prognosis [23,25]. The third phase is defined as pulmonary fibrosis [25]. However, the immunological defense mechanisms in other specific organs and tissues are still not completely understood [25].

In children, the manifestations of COVID-19 tend to be mild or the cases are asymptomatic [23]. The issue currently raised for this population is the presentation of an inflammatory syndrome that can lead to multiple organ failure and shock, described as multisystem inflammatory syndrome [5,26]. In these cases, clinical manifestations and laboratory changes were observed days or weeks after contact with SARS-CoV-2, suggesting that this syndrome may be a late complication recognized as a disproportionate immune response to infection [23,26].

In this context, to perform the diagnosis of COVID-19, currently the gold standard, which has better sensitivity and specificity, is the molecular test of reverse transcriptase polymerase chain reaction (RT-PCR) of nasopharyngeal samples, which aims detect the presence of SARS-CoV-2 RNA in the body [27,28]. The use of imaging tests aids in clinical suspicion and is useful for assessing the degree of pulmonary involvement by the disease, with findings suggestive of bilateral glass opacity dull or consolidation with thickening of the vascular interlobular septum of the peripheral areas of the lungs [27].

Regarding treatment, in mild cases, medication is recommended for symptomatic treatment, such as antipyretics for pain and fever, nutrition and adequate hydration [23]. For moderate and severe cases, treatment must be individualized [23].

ASSOCIATION OF MYOCARDITIS WITH COVID-19

Since the beginning of the SARS-CoV-2 pandemic, it has been noticed that children were less severely affected than adults, since they present an infection with clinical manifestations of mild respiratory symptoms [5,29,30]. However, in May of In 2020, pediatric centers in New York and European entities noticed a significant increase in children in need of intensive care units [5,29,31]. This is due to a severe inflammatory syndrome with characteristics similar to those found in Kawasaki disease [5,29,31].

With that, the WHO named this condition as multisystem inflammatory syndrome in children (MIS-C) related to COVID-19, and in view of these reports, a preliminary form was developed with both the definition and clinical and laboratory characteristics [5].

This inflammatory syndrome is characterized by a hyperinflammatory condition, which can cause multiple organ failure and shock [2,29,30]. It differs from classic Kawasaki in that it manifests more gastrointestinal symptoms, signs of hypoperfusion and systemic shock [2,29,30]. Furthermore, it is capable of causing cardiac endothelial cell dysfunction, leading to cardiac involvement [29,32,33].

Studies indicate that the onset of this syndrome occurs approximately three weeks after infection with SARS-CoV-2, since most patients have evidence of IgG class antibodies and few have positive RT-PCR [2,3,6,34].

Regarding cardiac involvement, myocarditis has been observed more frequently than usual. A prospective observational stud conducted in France to describe the characteristics of MIS-C by SARS-CoV-2 identified myocarditis in 76% of cases [35]. A second study, carried out in 7 hospitals in Paris, noted seven cases in sixteen patients [36]. An interesting fact also reported by Dufort et al in New York, where myocarditis was observed in 53% of cases [6].

To date, the pathophysiological evidence is still inconclusive regarding multisystem inflammatory syndrome and COVID-19 [26,31]. One of the hypotheses regarding COVID- 19-associated myocarditis is that the virus, like all betacoronaviruses, has a tropism for endothelial and myocardial cells as well as pulmonary and gastrointestinal tract cells [7,8]. Viral entry into the cell is facilitated by the binding of a spike protein to the angiotensin-converting enzyme 2 (ACE2) receptor [7,8]. The presence of the virus triggers a local inflammatory reaction with infiltration of T and B lymphocytes [7,8]. The tropism by myocardial cell occurs to varying extents during acute infection, even if the condition remains subclinical [7,8].

The early clinical phase of myocardial infection, viral propagation within myocardial cells causes cellular damage and exposure of cryptic antigens in the systemic circulation, such as cardiac myosin, which can lead to an autoimmune response [7]. Regardless of the patient's condition, some may enter a second phase, related to exacerbated inflammation in the cardiac tissue even after the complete elimination of the viral infection, a post-infectious myocarditis [7]. Persistence of cell damage may eventually progress to dilated cardiomyopathy and tissue fibrosis [7].

With this, the cardiac involvement associated with COVID-19 is identified in patients who, in most cases, need hospital care as a result of developed sequelae, since myocarditis can start abruptly and intensely, with severe and difficult heart failure. control. This is due to the development of transient left ventricular dilation

and therefore reduced ejection fraction by systolic dysfunction [6,29,37]. In addition, pericardial effusion, mitral regurgitation, and even coronary aneurysm may occur, which is seen with some frequency [7,29,35].

In the presentation of this syndrome, high and persistent fever (38 to 40°C), exanthemas of varied presentations, non-purulent conjunctivitis, edema of hands and feet, abdominal pain and diarrhea are reported [26,31]. The alterations in the laboratory tests, an increase in the values of C-reactive protein, procalcitonin, ferritin, D-dimer and myocardial function tests were observed [26].

TREATMENT

Management begins with the treatment of MIS-C by a multidisciplinary team, since the pathophysiological mechanism is not fully understood [2,6,35,37]. It is known to date that most cases require intensive care unit therapy due to cardiovascular dysfunction, which can progress to severe hypotension and shock [2,3,6,35,37].

Regarding SARS-CoV-2 myocarditis, studies indicate that many patients require intravenous inotropic support, in addition to fluid resuscitation [2,3,6,35,37].

On the other hand, mechanical ventilation was often instituted aiming at better cardiovascular support than respiratory support [2,3,6,35,37]. In addition, for the treatment of MIS-C, the most used therapy was intravenous immunoglobulin associated with the use of glucocorticoids, especially in more severe patients [2,3,6,35,37]. However, interleukin inhibitors have had their use restricted, although they can be used as a second option [2,3,6,35,37].

Prophylactic anticoagulation was cited as essential for the management of hospitalized patients, especially those with left ventricular dysfunction, arrhythmias or coronary artery involvement [2,3,6,35,37]. As a first line of prevention, low molecular weight heparin was the most indicated, but always considering interactions with other drugs used in therapy [2,3,6,35,37].

Due to the higher risk of shock in this syndrome, the use of ECMO was considered early [3,6,35,37]. Finally, there is still no specific protocol for the treatment of myocarditis after COVID-19 for pediatric patients in the literature [2,3,6,35,37].

DISCUSSION & CONCLUSION

Viral myocarditis is the main etiology of the pathology whose mechanism is inflammation and necrosis of the heart muscle in the absence of an ischemic event. Despite the mostly favorable outcomes of the disease in the pediatric population, it is notable that it causes important morbidities and even death. Therefore, it is essential that the clinician be able to suspect and diagnose myocarditis early, in order to avoid progression to severe and irreversible heart failure.

With the new coronavirus pandemic, the uncertainties regarding the therapeutic approach of patients who have the multisystem inflammatory syndrome caused by the disease and, therefore, have myocardial involvement are evident. It is observed that current therapeutic measures aim to provide symptomatic support, but the underlying cause is not treated.

Finally, it is concluded that additional studies are required to better understand the pathophysiology involving the new coronavirus and myocyte injury, as well as further clarifications regarding the therapeutic approach for the affected children.

ACKNOWLEDGEMENT

Schinke MR, Martins LO, Goetten A, Gomes CS and Carneiro JL S participated in research and development the manuscript. Assahide MHK guided the entire process. All authors participated in the revisions of the manuscript, read and approved the final version of this article.

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